THE USEFULNESS OF PLEURAL FLUID URIC ACIDAND ITS RATIO TO SERUM URIC ACID LEVELS IN CLASSIFYING PLEURAL EFFUSIONS AS EXUDATES AND TRANSUDATES AND ITS CORRELATION WITH LIGHT'S CRITERIA

DISSERTATION SUBMITTED FOR

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CERTIFICATE FROM THE DEAN

This is to certify that this dissertation entitled **"THE USEFULNESS OF PLEURAL FLUID URIC ACID AND ITS RATIO TO SERUM URIC ACID LEVELS IN CLASSIFYING PLEURAL EFFUSIONS AS EXUDATES AND TRANSUDATES AND ITS CORRELATION WITH LIGHT'S CRITERIA"** is the bonafide work of **Dr. P.KARUPPASAMY,** in partial fulfilment of the university regulations of the Tamil Nadu Dr. M.G.R. Medical University, Chennai, for M.D General Medicine, Branch I examination to be held in May 2018.

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I, **Dr.P.KARUPPASAMY**, solemnly declare that this dissertation titled **"THE USEFULNESS OF PLEURAL FLUID URIC ACID AND ITS RATIO TO SERUM URIC ACID LEVELS IN CLASSIFYING PLEURAL EFFUSIONS AS EXUDATES AND TRANSUDATES AND ITS CORRELATION WITH LIGHT'S CRITERIA"** is a bonafide record of work done by me at the Department Of General Medicine, Government Rajaji Hospital, Madurai, under the guidance of **Dr.G.BAGIALAKSHMI, M.D.,** Professor, Department of General Medicine, Madurai Medical college , Madurai.

This dissertation is submitted to The Tamil Nadu Dr. M.G.R Medical University, Chennai in partial fulfilment of the rules and regulations for the award of M.D Degree General Medicine Branch- I examination to be held in May 2018.

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CONTENTS

INTRODUCTION

INTRODUCTION

Pleural effusion is a very common clinical presentation of diseases. A correct diagnosis of the underlying disease is essential for the management of pleural effusion. A limited number of diseases cause Transudative Pleural Effusion, whereas exudative effusions require more extensive diagnostic investigations. Therefore, the first step is to classify them as transudates or exudates, even if this differentiation does not contribute to the etiological diagnosis.

Many criteria have been used to distinguish them, but none of them have been found to be satisfactory. Light's criteria is the most commonly used method

"The criteria is one or more of the following to diagnose exudates.

1. Pleural fluid protein / Serum protein>0.5
2. Pleural fluid LDH/ Serum LDH >0.6
3. Pleural fluid LDH more than 2/3rd of the upper limit of serum"

LDH.

It was found that even Light's criteria misclassified a large number of effusions - 25% of transudates as exudates.

Hence, there is a need to find new parameters which will prove to be superior or supportive to the various investigations available at present. Many other biochemical markers like bilirubin, cholesterol, Uric acid, etc. can be taken into consideration.

Hence, this study is done to evaluate the efficacy of Total Pleural fluid Uric acid and its ratio to Serum Uric acid levels in classifying the Pleural Effusion as Exudate or Transudate and its correlation with Light's criteria.

AIMS AND OBJECTIVES

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To evaluate the advantages of Total Pleural fluid Uric acid and its ratio to Serum Uric acid levels in classifying Pleural Effusions as Exudates or Transudates.

REVIEW OF LITERATURE

REVIEW OF LITERATURE

Definition

Pleural effusion is defined as the abnormal accumulation of pleural fluid within the pleural cavity. Crucial feature of the breathing apparatus is the pleural space. This is a potential space between the parietal pleura and the visceral pleura.It is the coupling system between the lung and the chest wall.

ANATOMY OF PLEURA

The lung parenchyma, the diaphragm, the mediastinum and the rib cage are covered by a serous membrane called the Pleura. Pleura is divided into visceral pleura and parietal pleura. Both these layers meet at the lung root.

Visceral pleura

It covers the lung parenchyma in its points of contact with the diaphragm, the mediastinum and the chest wall and also in the inter-lobar fissures

Parietal pleura

It lines the inside of the thoracic cavities.

It is subdivided on the basis of intra-thoracic structures that it lines into

1. Costal parietal pleura
2. Mediastinal parietal pleura
3. Diaphragmatic parietal pleura.

Pulmonary ligament

This is a thin double fold of pleura formed due to the downward extension of the pleura, posterior to the lung root.

Pleural space

This is a potential space present between the visceral and parietal pleura.

Pleural fluid

This is a thin film of fluid normally present in between the visceral pleura and parietal pleura i.e., pleural space

Functions of pleural fluid: It acts as a lubricant. During the respiratory movements the pleural fluid facilitates the visceral pleura which is covering the lung to slide along the parietal pleura which lines the thoracic cavity.

HISTOLOGY OF PLEURA

Parietal pleura and visceral pleura are composed of two layers, namely the mesothelium and the connective tissue.

Functions of Connective tissue layer

1. Contributes to elastic recoil of lung and helps in expelling air from the lung
2. Restricts the inflatable volume of lung and thereby protects the lung.

Functions of Mesothelial cells

It forms a monolayer of pavement like cells lining the pleural surfaces.

1. Movement and transport of particulate matter and fluid across the pleural surfaces.
2. Migration of leucocytes in response to inflammation.
3. Synthesis of cytokines, growth factors, extracellular matrix proteins.
4. Antigen presentation and transformation to myofibroblasts.

Blood supply

Parietal pleura receives blood supply from systemic capillaries namely intercostal artery, pericardiophrenic artery, superior phrenic and musculophrenic artery and drained by intercostal veins and phrenic veins.

Visceral pleura: Pulmonary circulation supplies thin pleura and Bronchial arteries supply thick pleura. Venous drainage is through the pulmonary veins.

Lymphatic drainage

Lymphatic plexus in the parietal pleura drains into intercostal, mediastinal, tracheobronchial, parasternal and phrenic nodes.

In the parietal pleura the lymphatic vessels are in communication with the stomas, the diameter of which ranges between 2 to 6 microns. The main pathway for the elimination of particulate matter is the stomas with lacuna and lymphatic vessels.

In the visceral pleura there are abundant lymphatic vessels which join bronchial lymph vessels.

Nerve supply

Intercostal nerves supply the costal and peripheral part of diaphragmatic pleura. So the pain sensation due to inflammation of this part of pleura is perceived in the chest wall.

Phrenic nerve supplies the central part of diaphragmatic pleura. So when this part of pleura is irritated or inflamed the pain is felt in the ipsilateral shoulder.

PHYSIOLOGY OF PLEURA

Formation of the Pleural Fluid:

Pleural fluid can originate in the

- pleural capillaries
- intra-thoracic lymphatics
- intrathoracic blood vessels
- peritoneal cavity or
- interstitial spaces of the lung

Pleural Capillaries

The movement of fluid between the pleural capillaries and the pleural space obeys the Starling's law of transcapillary exchange.

Hydrostatic pressure

In the parietal pleura, the hydrostatic pressure is approximately 30 cm H2O,but the pleural pressure is approximately -5 cm H2O. The net hydrostatic pressure is therefore 30 - (-5) = 35 cm H2O.This pressure favours the movement of fluid from the capillaries in the parietal pleura to the pleural space.

Oncotic pressure

The hydrostatic pressure gradient is opposed by oncotic pressure gradient. Plasma oncotic pressure is approximately 34 cm H_2O.

Normally, the pleural fluid has an oncotic pressure of approximately 5 cm H_2O, as it contains a small amount of protein .The net oncotic pressure gradient is 34 - 5 = 29 cm H_2O. Thus, the net gradient is 35 - 29 = 6 cm H_2O. It favours the movement of fluid to the pleural space from the capillaries present in the parietal pleura.

The net gradient for fluid movement across the visceral pleura in humans is probably close to zero, which has not been demonstrated. The pressure in the parietal pleural capillaries is approximately 6 cm H2O more than that in the visceral pleural capillaries.

This is because capillaries in the visceral pleural are drained by the pulmonary veins. This is the only pressure that differs from the pressure affecting fluid movement across the parietal pleura. The net gradient for the parietal pleura

is 6 cm H2O. So the net gradient is approximately zero for fluid movement across the visceral pleura.

The capillaries in the visceral pleura are much farther from the pleural space when compared to the capillaries in the parietal pleura. Hence the filtration coefficient (Lp) for the visceral pleura is substantially less than that for the parietal pleura.

The fluid formation is more across the parietal pleura over the ribs than the pleura over the intercostal spaces. Also fluid formation was more over the caudal ribs than over the cranial ribs. But in contrast, pleural liquid absorption was more primarily in the parietal pleura adjacent to the intercostal space rather than that overlying the ribs. The formation of pleural fluid was more, if the breathing frequency was increased.

Interstitial Origin

It has been demonstrated that the interstitial spaces of the lungs is the origin of much of the fluid that enters the pleural space. Pleural fluid accumulates if there is either high-pressure or high-permeability pulmonary edema. The elevation in the wedge pressure is directly related to the amount of pleural fluid formed. But increased pleural fluid accumulation occur only after the development of pulmonary edema. The origin of the pleural effusion is probably the pulmonary interstitial space in patients with congestive heart failure,

It is likely that in many conditions associated with lung injury, such as lung transplantation and pulmonary embolisation, the origin of the pleural fluid is also the interstitial spaces of the lung.

It has been shown that the subpleural interstitial pressure increases with increasing levels of interstitial fluid. Even though the visceral pleura is thin, the barrier to the movement of fluid across the visceral pleura appears to be weak. Hence, once there is increase in subpleural interstitial pressure, the fluid will enter to the pleural space through the visceral pleura.

Peritoneal Cavity

If there is free fluid in the peritoneal cavity, pleural fluid accumulation can occur. Peritoneal fluid enters the pleural space through the openings in the diaphragm. Since the pressure in the pleural cavity is less than the pressure in the peritoneal cavity the fluid will flow from the peritoneal space to the pleural space. In conditions like hepatic hydrothorax, Meigs' syndrome, and peritoneal dialysis, the peritoneal cavity is the origin of the pleural fluid

Thoracic Duct or Blood Vessel Disruption

If there is disruption of thoracic duct, there is accumulation of lymph in the pleural space. This will produce a chylothorax. The rate of fluid accumulation can be more than 1,000 mL/day in chylothorax.

Origin of Normal Pleural Fluid

Pleural fluid is formed from the parietal pleural capillaries. The amount of pleural fluid formed daily is approximately 15 mL in a 50-kg individual. Since the protein level in the interstitial spaces is normally approximately 4.5 g/dL, and the protein level in normal pleural fluid is only approximately 1 to 1.5 g/dL, the origin of the fluid does not appear to be the interstitial spaces of the lung. Pleural fluid with lower protein levels are produced by higher vascular pressures. Evans blue dyed albumin studies with rabbits have demonstrated that most fluid originates in the parietal pleura over the ribs.

Pleural Fluid Absorption

Lymphatic Clearance

The lack of fluid accumulation in normal individuals is due to the clearance of fluid through the pleural lymphatics. The pleural space communicates with the lymphatic vessels in the parietal pleura via stomas in the parietal pleura. Visceral pleura lacks such stomas. The lymphatics in the parietal pleura removes proteins, cells and all other particulate matter from the pleural space. The carbon particles exit the pleural space through the stomas where the mesothelial cells are small and not flattened. Increased levels of nitric oxide in the pleural space cause increase in diameter of the stomas.

In a 60-kg individual the lymphatic drainage from each pleural space is on the order of 20 mL/hr or 500 mL/day.

Once the volume of the pleural liquid exceeds a particular threshold, the lymphatics operate at maximum capacity.

Clearance through Capillaries in Visceral Pleura

Until the mid-1980s, it was thought that the capillaries in the visceral pleura in humans were the primary route for the exit of fluid from the pleural space.

Through the lymphatics in the parietal pleura almost all the pleural fluid is removed. Several hundred millilitres of water probably traverse the pleural membranes each day. The net movement is of only a few millilitres as the osmolarity is nearly identical on each side of the membrane.

Alternative Mechanisms for Pleural Fluid Removal

Transcytosis plays a role in the removal of protein from the pleural space. Only 29% of the overall removal of albumin occurred through the stoma with small hydrothoraces, while 64% of the albumin from large hydrothoraces was removed through the stoma.

Pathogenesis of Pleural Effusions

Pleural effusion occurs whenever the rate of pleural fluid formation exceeds the rate of pleural fluid absorption.

Normally, a small amount (0.01 mL/kg/hour) of fluid constantly enters the pleural space from the capillaries in the parietal pleura. The lymphatics in the parietal pleura remove almost all of this fluid. Lymphatics have a capacity to

remove at least 0.20 mL/kg/hour. The lymphatics remove the fluid exceeding the normal rate of fluid formation by a factor of 20.

GENERAL CAUSES OF PLEURAL EFFUSION

A. Increased pleural fluid formation:

1. “Increased interstitial fluid in lungs
    - Left ventricular failure
    - Pneumonia
    - Pulmonary embolism
2. Decreased pleural pressure
    - Lung atelectasis
    - Elastic recoil of lung is increased
3. Increased permeability of pleural capillaries
    - Pleural inflammation
    - Elevated vascular endothelial growth factor (VEGF) levels
4. Increased levels of protein in the pleural fluid
5. Increased intravascular pressure in pleura
    - Right or left ventricular pressure
    - Superior vena cava syndrome
6. Disruption of thoracic blood vessels
7. Thoracic duct disruption
8. Increased fluid in the peritoneal cavity
    - Peritoneal dialysis
    - Ascites“

B. Decreased pleural fluid absorption

1. “Obstruction of pleural lymphatic drainage
2. Disruption of Aquaporin system in the pleura
3. Elevated systemic vascular pressure
    - Superior vena cava syndrome
    - Right ventricular failure”

1. Increased Pleural Fluid Formation

Whenever there is increased pulmonary interstitial fluid or when one of the terms in Starling's equation is changed, there is increased pleural fluid formation.

a) Increased Interstitial Fluid

Increased interstitial fluid in the lungs is the most common cause of increased pleural fluid formation. Irrespective of whether the edema is due to low-protein or high-protein fluid, pleural fluid accumulates whenever the amount of edema in the lung exceeds 5g/gram of dry lung weight. In conditions like congestive heart failure, parapneumonic effusions, acute respiratory distress syndrome, and in those who have undergone lung transplantation, increased interstitial fluid appears to be the predominant mechanism for the accumulation of pleural fluid.

b) Increased Hydrostatic Pressure Gradient

According to Starling's equation, there will be an increase in the rate of pleural fluid formation if there is an increase in the gradient between the intravascular pressure and the pleural pressure.

In conditions like right ventricular failure, left ventricular failure, pericardial effusion or superior vena cava syndrome, there is increase in the intravascular pressure. Atelectasis of the lower lobe or complete lung due to bronchial obstruction is the most common situation producing a decrease in the pleural pressure. A decrease in the pleural pressure also occurs when the visceral pleura becomes coated with a collagenous peel and the lung becomes trapped. The pleural pressure can become very negative, in these instances i.e., it goes below -50 cm H_2O. "The decreased pleural pressures can also contribute to pleural fluid accumulation in diseases where the elastic recoil of the lung is increased."

c) Increased Capillary Permeability

If the pleural surfaces become inflamed, the permeability of the capillaries may be increased. High levels of vascular endothelial growth factor (VEGF) increases the capillary permeability .This may be at least partially responsible for the accumulation of pleural fluid. It has been demonstrated that mesothelial cells have VEGF receptors on their surface. The levels of VEGF are higher in exudative than transudative pleural effusion.

d) Decreased Oncotic Pressure Gradient

In conditions like hemothorax, increased permeability pulmonary edema and with conditions in which the pleural capillary permeability is increased, the level of pleural fluid protein is increased. The capacity to remove pleural fluid by the lymphatics is approximately equal to the rate of formation of pleural fluid. Hypoproteinemia is a very uncommon cause of pleural effusion.

e) Presence of Free Peritoneal Fluid, or Disruption of the Thoracic Duct or an Intrathoracic Blood Vessel:

The free fluid in the peritoneal cavity traverse through the holes in the diaphragm and it leads to pleural fluid accumulation and pleural effusion. Similarly, if the thoracic duct disrupts, chyle will accumulate in the pleural space. And if there is a disruption of a blood vessel in the thorax, blood will accumulate in the pleural space.

2. Decreased Pleural Fluid Absorption

a) Normal Pleural fluid absorption by lymphatics

Normally, the lymphatic flow from the pleural space is approximately 0.01 mL/kg/hour or 15 mL/day as this is the amount of pleural fluid formed.

However, the capacity of the lymphatics is approximately 0.20 mL/kg/hour or 300 mL/day

b) Obstruction of Lymphatics

Obstruction of the lymphatics draining the parietal pleura is the most common cause of decrease in pleural fluid absorption. Lymphatic blockade is an important factor in the development of a malignant pleural effusion.

c) Elevation of Systemic Venous Pressures

Lymphatic flow will be reduced when there is elevation of pressure in the central veins. This is because the lymphatics drain into the systemic venous circulation.

The pleural effusions developed because of (a) leakage of lymph out of the lymphatics that pass through the chest (these include the diaphragmatic and pulmonary lymphatics and thoracic duct) ; or (b) leakage of interstitial fluid into the pleural space due to obstruction of lung or chest wall lymphatics .

CLINICAL MANIFESTATIONS OF PLEURAL EFFUSION

Normally, the pleural space contains only a few millilitres of pleural fluid. If fluid in the pleural space is detected on a radiologic examination, it is abnormal. Pleural fluid accumulation is associated with many conditions. When pleural fluid is detected, an effort should be made to determine the etiology.

1. Symptoms

In a patient with pleural effusion, symptoms mainly depends on the underlying process causing the effusion. Many patients have no symptoms referable to the effusion. When symptoms are related to the effusion, they arise either from inflammation of the pleura, compromise of pulmonary mechanics, interference with gas exchange, or rarely decreased cardiac output.

a) Pleuritic chest pain

Normally visceral pleura does not have pain fibres, only the parietal pleura contains pain fibres. In a patient with pleural effusion, pleuritic chest pain always indicates inflammation of the parietal pleura. Some patients with pleural effusions experience a dull aching chest pain rather than pleuritic chest pain.

The parietal pleura is innervated mostly by the intercostal nerves. So, the pain associated with pleural disease is well localized and it coincides with the area of the pleura which is affected by disease. Since the intercostal nerves are also distributed to the abdomen, pleuritic pain is referred to the abdomen .When the central portion of the diaphragmatic pleura is involved, there are exceptions to the localization of the pain. Phrenic nerve supplies this portion of the parietal pleura. Pain is referred to the tip of the ipsilateral shoulder if the central portion of the diaphragm is inflamed. Pleuritic pain felt simultaneously in the lower chest and ipsilateral shoulder points to diaphragmatic involvement

b) Cough

A dry, non-productive cough is the second symptom of pleural effusion. Although it may be related to pleural inflammation, the exact mechanism producing the cough is not clear. Alternately, cough reflex is stimulated by the pleural fluid compressing the lung, bringing the opposing bronchial walls into contact.

c) Dyspnea

Dyspnea is the third symptom of pleural effusion. As pleural effusion acts as a space-occupying process in the thoracic cavity, it reduces all subdivisions of lung volumes leading to dyspnea.

This explains the small increase in pulmonary function following therapeutic thoracocentesis if pleural effusion is associated with parenchymal disease. The degree of dyspnea is frequently out of proportion to the size of the pleural effusion.

Due to the weight of fluid on the diaphragm, the diaphragmatic function is compromised and this results in dyspnea.

2. Physical Examination

a) Inspection

Clinical findings vary according to the pleural pressure. The ipsilateral hemithorax will be larger and the usual concavity of the intercostal spaces will be blunted or even convex, if the pleural pressure on the side of the effusion is increased". In contrast, the ipsilateral hemithorax will be smaller and the normal concavity of the intercostal spaces will be exaggerated if the pleural pressure on the side of the effusion is decreased. This occurs with obstruction of a major bronchus or a trapped lung. In addition, the intercostal spaces retract with inspiratory efforts.

An indication of therapeutic thoracocentesis is enlargement of the hemithorax with bulging of the intercostal spaces. It is done to relieve the increased pleural pressure. It is also found that the hemithoraces are equal in size and the intercostal spaces are normal, in many patients with pleural effusions.

b) Palpation

Palpation is useful to determine the extent of the effusion. Vocal fremitus is absent or attenuated in areas of the chest where pleural fluid separates the lung from the chest wall. This is because the vibrations emanating from the lung are absorbed by the fluid.

To identify the upper limit of the pleural fluid, vocal fremitus is much more reliable than percussion. It is also useful to identify a proper site to attempt a thoracocentesis. Vocal fremitus is much more reliable than percussion, because with a thin rim of fluid, the tactile fremitus is diminished, but the percussion note may still be resonant.

Apical impulse

Palpation may also reveal that the apical impulse is shifted to one side or the other. The apical impulse may not be palpable in patients with large left pleural effusions.

Position of trachea

The position of the trachea in patients with pleural effusion always indicates the relationship between the pleural pressures in the two hemithoraces.

c) Percussion

In a patient with pleural effusion the percussion note over the area of involvement is dull or flat. For identifying small amounts of pleural fluid, light percussion is better than heavy percussion.

d) Auscultation

Auscultation reveals decreased or absent breath sounds. However, breath sounds may be accentuated and take on a bronchial characteristic, near the superior border of the fluid. This accentuation of breath sounds denotes a passively collapsed lung with a communicating bronchus.

Systemic cause and clinical findings

1. If the patient has cardiomegaly, neck vein distension, or peripheral edema, the effusion is probably due to congestive heart failure (CHF).
2. The pleural effusion is due to rheumatoid disease or systemic lupus erythematosus (SLE) if the patient has signs of joint disease or subcutaneous nodules.
3. Metastatic disease such as breast masses should be suspected as the cause of pleural effusion if there is an enlarged, nontender nodular liver or the presence of hypertrophic osteoarthropathy.
4. In patients with subdiaphragmatic pathology there will be abdominal tenderness.
5. Tense ascites suggests cirrhosis and a hepatic hydrothorax.
6. Lymphoma, sarcoidosis or metastatic disease should be suspected if there is lymphadenopathy.

DIFFERENTIAL DIAGNOSIS OF PLEURAL EFFUSION

1. Transudative pleural effusions

A. Congestive heart failure

B. Cirrhosis

C. Nephrotic syndrome

D. Cerebrospinal fluid leaks to pleura

E. Hypoalbuminemia

F. Peritoneal dialysis

G. Glomerulonephritis

H. Constrictive pericarditis

I. Myxoedema

J. Superior vena cava obstruction

K. Urinothorax

2. Exudative pleural effusions

A. Neoplastic diseases

1. Metastatic disease

2. Mesothelioma

3. Pyothorax-associated lymphoma

4. Body cavity lymphoma

B. Infectious diseases

1. Bacterial

2. Tuberculosis

3. Viral

4. Parasitic

5. Fungal

C. Pulmonary embolization

D. Gastrointestinal disease

1. Pancreatic disease

2. Subphrenic abscess

3. Intrahepatic abscess

E. Obstetric and gynecologic disease

1. Ovarian hyperstimulation syndrome

2. Fetal pleural effusion

3. Endometriosis

4. Postpartum pleural effusion

5. Meigs' syndrome

F. Collagen vascular diseases

1. Rheumatoid pleuritis

2. Systemic lupus erythematosus

3. Sarcoidosis

G. Drug-induced pleural disease

1. Ergot drugs

2. Amiodarone

3. Interleukin 2

4. Nitrofurantoin

5. Dantrolene

6. Methysergide

I. Hemothorax

J. Chylothorax

GENERAL TO DIFFERENTIATE THE CAUSES OF EXUDATIVE PLEURAL EFFUSION:

1. Appearance of the fluid

Most pleural effusions are clear, straw colored, nonviscid and odourless. The red colour of the fluid indicates the presence of blood. To confirm hemothorax, a hematocrit should be done. If the hematocrit of the pleural fluid was more than 50

% of the peripheral blood hematocrit, then it is a hemothorax. When the pleural fluid is blood tinged the RBC count is 5000 to 10000 / mm3 . If the pleural fluid macrophages contain haemoglobin inclusions, then it indicates that the blood was present before thoracocentesis and the blood is not due to traumatic tap.

Increased lipid content or increased cellular content both can make pleural fluid to appear turbid. If after centrifuge the supernatant fluid remains turbid then it is due to lipid content.

Amebiasis with a hepato-pleural fistula – chocolate sauce or anchovy sauce pus is seen. The mixture of blood, cytolysed and normal liver tissue make this appearance.

Malignant mesothelioma	–	High viscosity due to elevated hyaluronic acid
.Anaerobic bacterial infection	–	Faeculent odour
Urinothorax	–	Smell of urine

2.WBC count

Most transudates have WBC count below 1,000/mm3 and exudates have more than 1,000/mm3.”

WBC count > 10,000/mm3 – parapneumonic effusions

WBC count > 50,000/mm3 – pancreatic disease and pulmonary embolism Neutrophils predominate – suggests acute inflammation. It is seen in pneumonia, pancreatitis, pulmonary embolism, subphrenic abscess and early tuberculosis.

Eosinophils predominate – indicates air or fluid in the pleural space. It is seen in patients with spontaneous pneumothorax who had undergone thoracotomy, introduction of air during thoracentesis into pleural space, traumatic hemothorax, pulmonary embolization, CABG, asbestos related effusion, drugs like dantrolene, bromocriptine, parasitic disease like amebiasis, ascariasis .

Basophils predominate – pneumothorax, pneumonia, leukemic pleural involvement

Pleural fluid lymphocytosis - malignancy, TB, CABG, leukemia or lymphomas. Mesothelial cells – Tuberculosis in HIV patients. Whereas it is absent in complicated parapneumonic effusions, malignancy after pleurodesis.

3. Glucose levels

Glucose level < 60 mg / dL – malignancy, parapneumonic effusions, rheumatoid pleuritis, tuberculosis. Other causes include hemothorax, lupus pleuritis, paragonimiasis, Churg-Strauss syndrome.

4. Amylase level

It is elevated in pancreatic disease, malignancy, esophageal rupture. In the last two conditions the amylase is of salivary type.

5. Lactate dehydrogenase level

LDH in the pleural fluid is a reliable indicator of degree of inflammation of the pleura. More the inflamed surfaces, higher the LDH levels. The most common causes of elevated LDH levels are parapneumonic effusions and malignancy. These two conditions mostly meet the light's criteria on the basis of levels of LDH than

the protein levels .The iso-enzymes elevated in these conditions are LDH – 4 and LDH – 5. They are thought to arise from the inflammatory WBCs.

Usually LDH isoenzyme is not used routinely. This is done in conditions where there is a bloody pleural fluid tap in a patient who has transudative pleural effusion clinically. The pleural fluid protein meets the criteria for transudative pleural effusion but LDH levels meet the criteria for exudative pleural effusion. In these conditions iso-enzyme LDH – 1 confirms that the rise in LDH was due to blood.

6. AdenosineDeaminase

ADA has two isoenzymes – ADA 1 and ADA 2

ADA 1 is produced by lymphocytes, neutrophils, monocytes, macrophages ADA 2 is produced by macrophages and monocytes.

The cut off level for ADA level to diagnose tuberculous pleural effusion is 40 to 45 U/L. The diagnosis of TB pleural effusion is more likely if the level is higher i.e., more than 70 U/L.

7. C–Reactive proteins more than 50 mg /L, high levels of **lysozyme** are also used to diagnose tuberculous pleuritis.

8. Lipids

Chylothorax-Accumulation of chyle in the pleural space due to disruption of the thoracic duct. In these situations the triglyceride levels are increased".

Chyliform pleural effusions – This is characterised by high levels of lecithin globulin levels.

Pseudo chylous effusions –There is increased levels of cholesterols crystals. Triglyceride levels more than 110 mg / dL – Chylothorax is confirmed.

But if the levels are less than 50 mg / dL then the patient does not have chylothorax.

If triglyceride level is between 50 to 110 mg / dL then a lipoprotein analysis should be done. Presence of chylomicrons in the lipoprotein analysis of pleural fluid is diagnostic of Chylothorax.

RADIOGRAPHIC EXAMINATION OF PLEURAL EFFUSION

Typical Arrangement of Free Pleural Fluid

The distribution of free fluid in the pleural spaceis governed by two important factors.

First, accumulation of the pleural fluid occurs in “the most dependent part of the thoracic cavity since the lung is less dense than pleural fluid.

Second, the distribution of fluid within the free pleural space obeys the law of gravity. The lung also maintains its shape when compressed.

Bearing these 2 factors in mind, it is easy to predict the distribution of excess pleural fluid.

The fluid first gravitates to the base of the hemithorax and comes to rest between the inferior surface of the lung and the diaphragm, where the pleural sinus is the most inferior, particularly posteriorly. The fluid spills out into the costophrenic sinuses posteriorly, laterally and anteriorly when the fluid accumulation is higher. Additional fluid assumes a higher position in the thorax as it spreads upward in a mantle-like manner around the convexity of the lung and gradually tapers.

The lateral costophrenic angle is obliterated in the posteroanterior projection. The density of the fluid is high laterally and curves gently medially and downward, to terminate at the mediastinum with a smooth, meniscus-shaped upper border. At the mediastinal border the layer of fluid is narrower than at the costal border.

The upper surface of the pleural fluid density is semicircular in the lateral projection. It is high in the anterior and posterior regions. It curves smoothly downward to its lowest point approximately midway between the posterior chest wall and the sternum.

Frequently, in the lateral chest radiograph a middle lobe step is observed. The explanation for the middle lobe step is that the most dependent and the first affected lobe is the lower lobe, the pleural fluid starts to accumulate here. Therefore, it starts to float and shrink but maintains its shape. So the middle

lobe is unaffected and its full volume is maintained. Hence, the result is a middle lobe that retains its usual size and shrunken lower lobe. The fluid

accumulation is mostly in the posterior part of the chest on radiograph. The height of the pleural fluid is greater laterally, based on the radiologic appearance. When viewed en face, this layer of fluid is of insufficient depth to cast a discernible shadow, so it assumes a meniscus shape.

Radiologic Signs

The fluid first accumulates between the inferior surface of the lower lobe and the diaphragm, when the patient is in the upright position. The pleural fluid occupies this position if the amount of fluid is small (approximately 75 mL) and without spilling into the costophrenic sinuses. The normal configuration of the diaphragm is maintained, with this small amount of fluid.

The chest radiograph when viewed in the lateral projection, accumulation of more fluid obliterates the costophrenic angle as it spills over into the posterior costophrenic angle. The posterior costophrenic angle is normally sharp. It is obliterated by a homogeneous, shallow shadow with a meniscus-shaped upper surface. There is also widening of the pleura that lines the posterior thoracic wall .

If the posterior part of one or both diaphragms is obscured or the posterior costophrenic angle is obliterated, it indicates the presence of pleural fluid.

Then we should be do further diagnostic tests.

The presence of clinically significant amounts of free pleural fluid can be nearly excluded, if both posterior costophrenic angles are clear and sharp. In the postero - anterior chest radiograph, lateral costophrenic angle is blunted with

increasing amounts of fluid. The entire outline of the diaphragm is lost on the affected side. as more fluid accumulates. The fluid then extends upwards around the posterior, anterior and lateral thoracic walls. At the lung base, this fluid produces opacification which is the typical meniscus shape.

Supine Position

There are three characteristics that serve to differentiate the increased density due to parenchymal infiltrate from that due to a pleural fluid.

First, in a properly exposed film, “the vascular structures of the lung will be readily visible through the density, if the density is caused by pleural fluid”. However, vascular structures are obliterated by the silhouette effect, if a similar density is produced by any intrapulmonary process.

Secondly, the density is usually completely homogenous, if it is due to pleural fluid. Whereas, the infiltrates are usually less homogenous, if it is caused by an intrapulmonary processes. Third, the presence of air bronchograms. They are present only if the increased density is due to a parenchymal infiltrate and not due to a pleural fluid

Ultrasound

In a pleural effusion, the ultrasound can be used for the following purposes. They are

1. To determine the presence of pleural fluid

2. To identify an appropriate location for the attempted thoracocentesis, chest tube placement, or pleural biopsy
3. To identify loculated pleural effusion
4. To distinguish pleural thickening from pleural fluid
5. To semi-quantify the amount of pleural fluid
6. To differentiate a lung abscess from a pyopneumothorax
7. to assess whether pleurodesis is present and
8. To evaluate the trauma patient for the presence of a pneumothorax or a hemothorax.

PICTURE

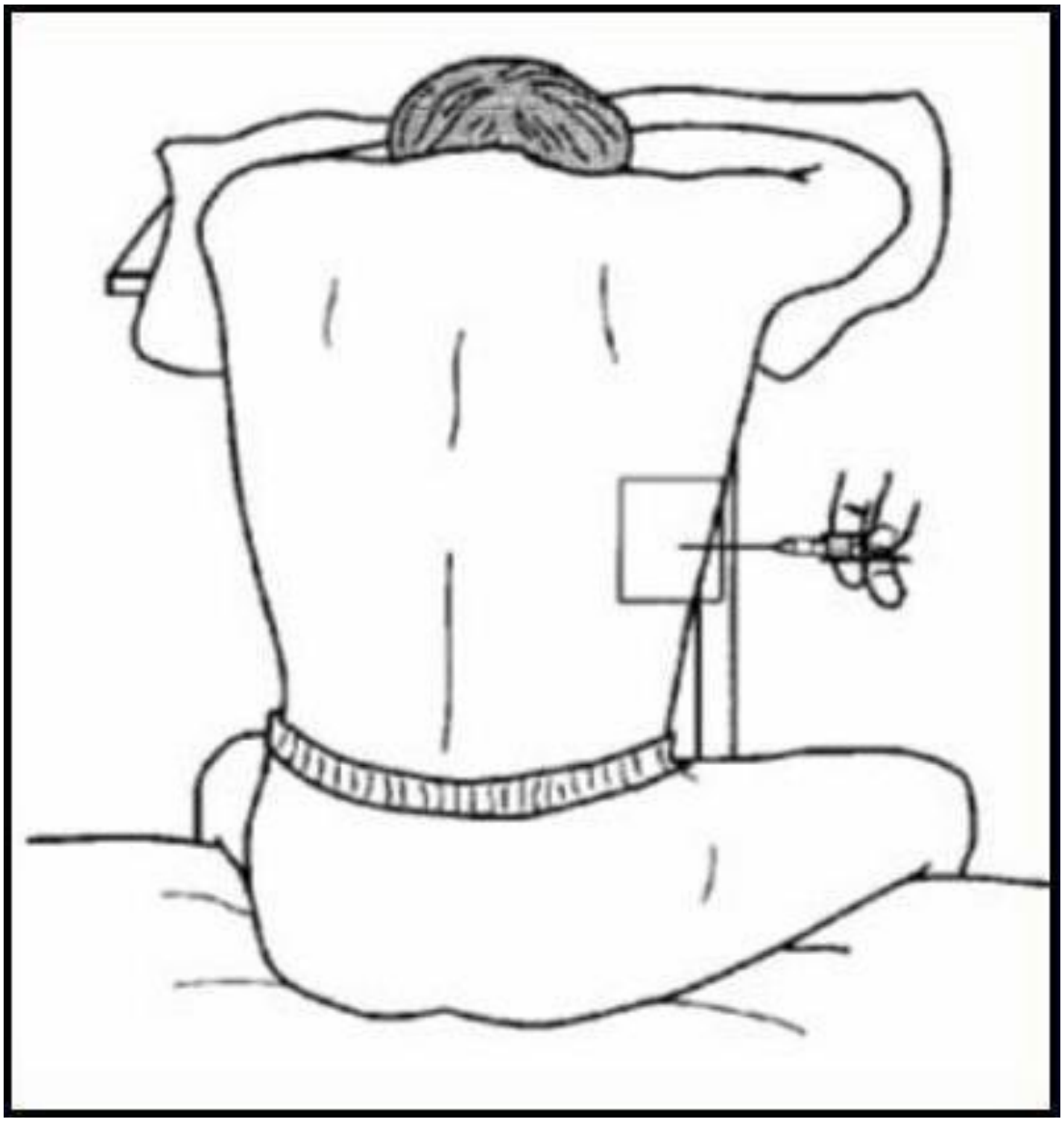
CHEST X RAY – POSTERIOR ANTERIOR [PA] VIEW SHOWING

RIGHT SIDED PLEURAL EFFUSION

FIGURE

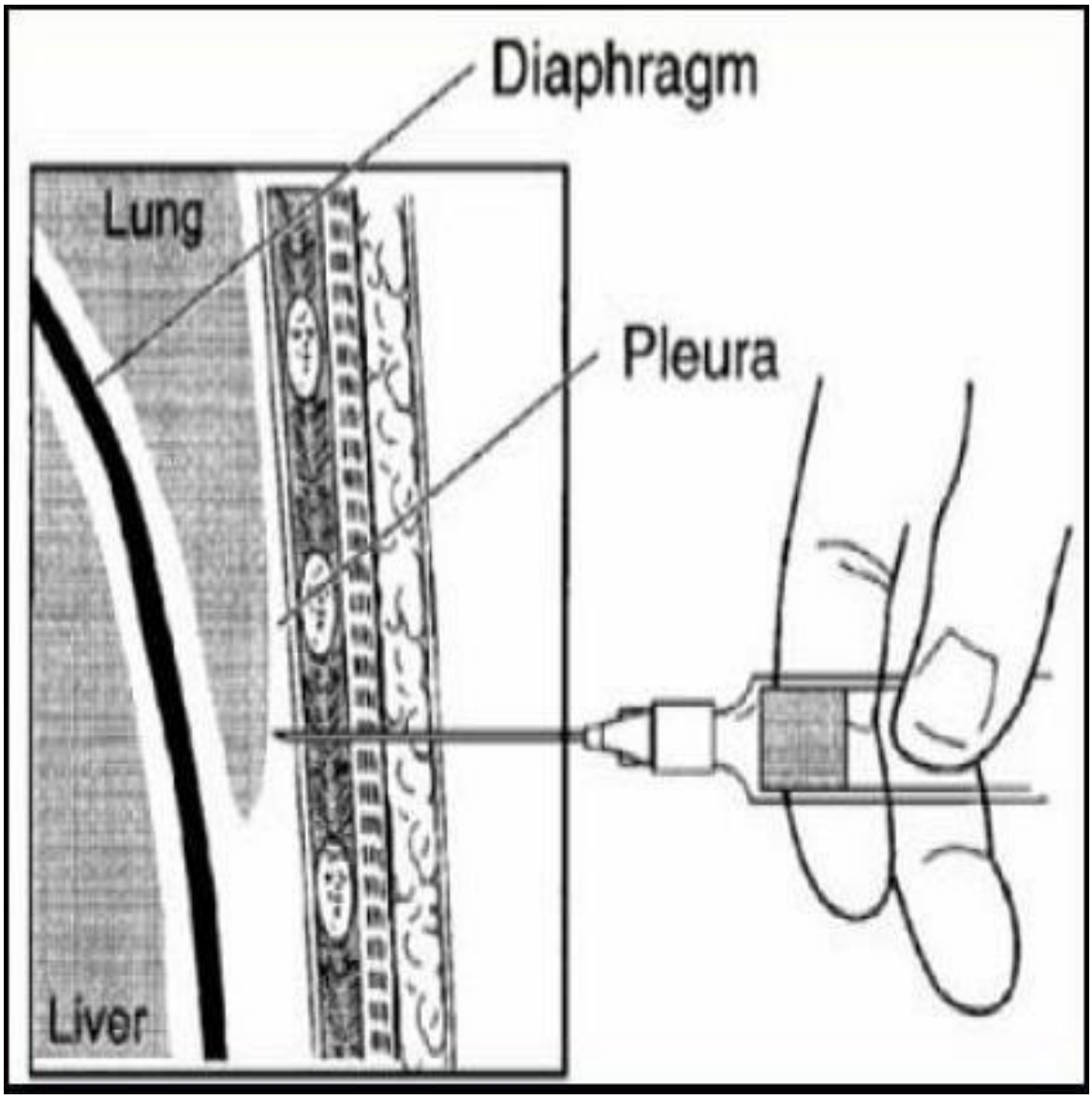
DIAGNOSTIC OR THERAPEUTIC THORACENTESIS

RECOMMENDED POSITION OF THE PATIENT



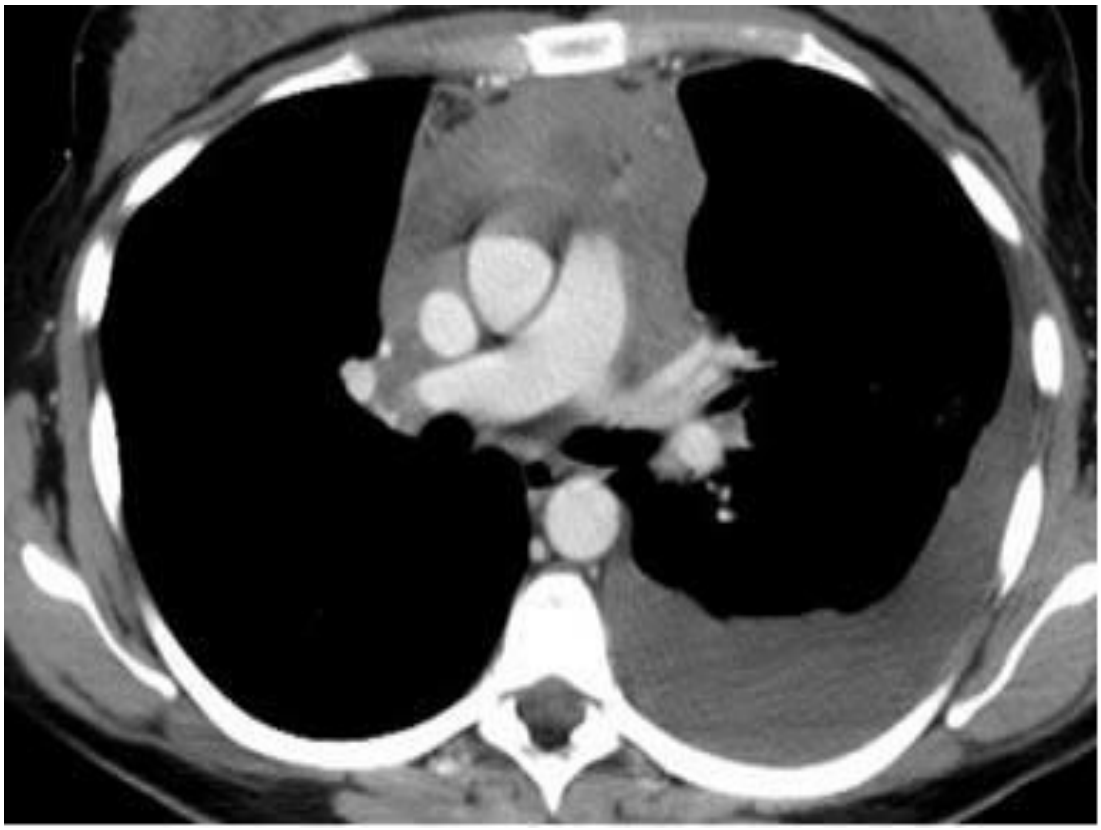
FIGURE

DIAGNOSTIC THORACENTESIS: THE PLEURAL SPACE IS ENTERED AND PLEURAL FLUID IS OBTAINED.



FIGURE

CT CHEST PLAIN SHOWING PLEURAL EFFUSION



SEPARATION OF TRANSUDATIVE FROM EXUDATIVE EFFUSIONS

The accumulation of clinically detectable quantities of pleural fluid is distinctly abnormal.

Indications of diagnostic thoracocentesis:

1. Whenever the thickness of pleural fluid on ultrasound or the decubitus radiograph is greater than 10 mm or
2. Whenever loculated pleural fluid is demonstrated with ultrasound
3. Etiology of the effusion is unknown.

A diagnostic thoracocentesis takes less than 10 minutes. It should not cause any morbidity more than a venipuncture. The information available from examination of the pleural fluid is invaluable in the management of the patient with pleural effusion.

Transudative pleural effusion

If the systemic factors influencing the absorption or formation of pleural fluid are altered, transudative pleural effusion develops.

The permeability of the capillaries to proteins, ALP, cholesterol is normal in the area where the fluid is formed.

Examples of conditions producing transudative pleural effusions;

1. Increased pulmonary interstitial fluid and a resulting pleural effusion - left ventricular failure.

2. Movement of fluid across the diaphragm from ascites due to cirrhosis.
3. Decreased serum oncotic pressure with hypoproteinemia.

Exudative pleural effusion

In contrast when the pleural surfaces or the capillaries in the location where the fluid originates are altered such that fluid accumulates, an exudative pleural effusion develops.

The common causes of exudative pleural effusions are:

1. Pleural malignancy,
2. Parapneumonic effusions,
3. Tuberculosis and
4. Pulmonary embolism.

Total protein

Earlier to separate between transudate and exudates, a pleural fluid protein of 3gms was used. This test misclassified about 10% of pleural effusions.

Light's criteria:

"Light demonstrated the following criteria for diagnosing exudate. Exudative pleural effusions meet at least one of the following criteria

- Pleural fluid protein divided by serum protein greater than 0.5
- Pleural fluid LDH divided by serum LDH greater than 0.6

- Pleural fluid LDH greater than two thirds of the upper limit of normal serum LDH".

Other tests to differentiate exudates and transudate

In recent years, following are the other tests for the separation of transudates from exudates.

1. Pleural fluid ALP > 60 IU'
2. Pleural fluid serum ALP ratio > 0.35,
3. Pleural fluid serum albumin gradient of <1.2.
4. Pleural fluid protein gradient <3.1.

When a pleural fluid shows above findings on analysis then it indicates an exudative effusion.

Light's criteria identify approximately 20% of transudative effusions as exudates. This "mislabeling occurs most commonly in patients with CHF. When they are treated with diuretics before thoracocentesis is performed, these mislabeled transudates barely meet the exudative criteria. The mislabeled transudate can be identified by examining the gradient between the serum and the pleural fluid protein levels." If this gradient is greater than 3.1 g/dL, one can presume that the fluid is actually a transudate. An albumin gradient of 1.2 g/dL rather than the protein gradient of 3.1 g/dL can be used.". However, the protein gradient is equally effective as the albumin gradient. Also the pleural fluid bilirubin and cholesterol,uric acid can be used to correctly identify the transudates and exudates.

Uric acid

"Uric acid is a metabolic end product of purine nucleotides, one of the biochemical marker found in pleural fluid, and is sparingly soluble in acqueous media and persistent exposure to high serum levels predispose to urate crystal formation within soft tissues and body fluids".. uric acid levels are" increase more in transudative pleural fluid (CCF, peritoneal dialysis, cirrhosis and nephrotic syndrome)than exudative condition." , "In exudative condition the local factors, influencing the accumulation of pleural fluid are altered. Exudates involve increased capillary permeability and lymphatic obstruction".

Whereas "transudates are the result of changes in hydrostatic forces [imbalances in hydrostatic and oncotic forces], with capillary permeability remaining normal".

The condition which produces transudative pleural effusion exerts oxidative stress and hypoxia in the tissues.It is stated that increases in uric acid level may be found in clinical conditions associated with tissue hypoxia

In our study to diagnose exudates the following parameters are used

A pleural fluid Uric acid of less than 5.45 IU

A pleural fluid Uric acid to serum Uric acid ratio of less than 0.45

Approach to diagnose a transudative or exudative pleural effusion

First assess the fluid for Light's criteria. The fluid is more likely an exudate if there is higher the value for the protein ratio, the LDH ratio, and the absolute value of the LDH. If the fluid meets the criteria for a transudative effusion, it is a transudate.

If the fluid meets the criteria for an exudative effusion by only a small margin and the clinical picture is compatible with a transudative effusion, measure the protein gradient between the serum and pleural fluid. If this value is greater than 3.1 g/dL, then the fluid can be relabelled a transudate.

Other Characteristics of Transudates

Most transudates are clear, straw coloured, non - viscid, and odourless. The discovery of blood-tinged pleural fluid does not mean that the fluid is not a transudate. To give the pleural fluid a pinkish tinge, pleural fluid red blood cell (RBC) count should be more than 10,000/mm3. Approximately 15% have RBC counts above this level. RBCs contain a large amount of LDH. So elevated LDH level in a blood-tinged or bloody transudative pleural effusion would meet the criteria for an exudative pleural effusion.

White blood cell (WBC) count

White blood cell (WBC) count in the pleural fluid of most transudates is less than 1,000/mm3, but approximately 20% have WBC counts that exceed 1,000/mm3. WBC counts in pleural fluid above 10,000/mm3 are rare in

transudative pleural effusions. The differential WBC count may be dominated by polymorphonuclear leukocytes, small lymphocytes, or other mononuclear cells in transudative pleural effusions.

In a series of 51 transudative effusions, 7 (13%) had more than 50% polymorphonuclear leukocytes, whereas 17 (34%) had predominantly small lymphocytes, 23 (47%) had predominantly other mononuclear cells, and 4(6%) had no single predominant cell type.

The glucose level in pleural fluid is similar to the serum glucose level, but the level of pleural fluid amylase is low. Because of active transport of bicarbonate from the blood into the pleural space, there is always higher pleural fluid pH in patients with transudative pleural effusions than the pH in simultaneously obtained blood

Diagnostic Thoracocentesis

If the decubitus film demonstrates presence of free pleural fluid, then one should consider performing a diagnostic thoracocentesis with the aid of ultrasound or with a CT scan. The thickness of the fluid is important in performing the diagnostic thoracentesis. It is difficult to perform a diagnostic thoracocentesis if the thickness of the fluid on the decubitus radiograph, ultrasound, or the CT scan is less than 10 mm. However, if the thickness of the fluid is greater than 10 mm, we have to consider performing a diagnostic thoracocentesis.

There is no need to perform diagnostic thoracentesis if the patient has congestive heart failure. But in a patient with congestive heart failure if any of the

following three conditions are met: (a) the patient is febrile (b) the effusions are not bilateral and comparably sized (c) the patient has pleuritic chest pain. a diagnostic thoracocentessis is done later, if the pleural effusions do not rapidly disappear. Otherwise, treatment of the congestive heart failure is initiated.

To sum up, the main aim of performing a diagnostic thoracentesis is to determine whether the patient has an exudative or a transudative pleural effusion.

TRANSUDATIVE PLEURAL EFFUSION

Alternation in the systemic factors influencing the formation and absorption of the pleural fluid leads to accumulation of the pleural fluid and formation of transudative pleural effusion.

The major causes are:

1. Congestive Heart Failure:

The most common cause of pleural effusion is probably the congestive heart failure (CHF). The incidence of pleural effusions in patients with CHF is high.

Pathophysiology

In patients with CHF, according to current theories on pleural fluid formation and reabsorption, there is a different entry pathway and a different exit pathway for pleural fluid.

It is believed that almost all fluid exits the pleural space through the lymphatics in the parietal pleura rather than by passively diffusing across the

visceral pleura. In patients with CHF, pleural effusion occurs when the rate of entry of fluid into the pleural space exceeds the capability of the lymphatics in the parietal pleura to remove the fluid.

Clinical Manifestations

In patients with pleural effusions due to CHF they are usually associated with other manifestations of that disease. The patient has a history of increasing dyspnea on exertion, orthopnea or paroxysmal nocturnal dyspnea, increasing peripheral edema. The dyspnea is frequently out of proportion to the size of the effusion.

Physical examination

Physical examination usually reveals signs of the pleural effusions as well as signs of both left-sided heart failure with an S3 ventricular gallop and rales and right-sided heart failure with peripheral edema and distended neck veins.

Investigations

The chest radiograph almost always reveals usually bilateral pleural effusion and cardiomegaly. Congestive heart failure is the most common cause of bilateral pleural effusion. But only 88% of the patients studied had bilateral pleural effusion, if cardiomegaly is not present.

The mean volume of pleural fluid in the right pleural space (1,084 mL) when compared to the mean volume of pleural fluid in the left pleural space (913 mL)

was only slightly greater. Also mediastinal lymphadenopathy is common in patients with pleural effusions that are secondary to CHF.

Diagnosis

If the patient has bilateral pleural effusions and cardiomegaly, not febrile and no history of pleuritic chest pain, we have to initiate treatment of CHF. Then we have to observe the patient and determine whether the pleural fluid is reabsorbed. A diagnostic thoracocentesis should then be done if the effusions do not disappear within a few days.

One problem with this approach is that the characteristics of the pleural fluid may change from those of a transudate to those of an exudate, since the patients are on diuretics

Serum pleural fluid albumin or protein gradient

The serum to pleural fluid protein gradient should be examined if the pleural fluid meets exudative criteria but the effusion is thought to be due to CHF. If this gradient is greater than 3.1 g/dL, additional diagnostic studies are not indicated because the pleural effusion is probably due to the CHF. Currently, as the protein gradient is already available when Light's criteria are measured, the protein gradient of 3.1 g/dL is preferred to the albumin gradient.

Pro-brain natriuretic peptide:

The measurement of the serum or pleural fluid pro-brain natriuretic peptide (pro-BNP) is another test that should be considered for establishing the diagnosis

of CHF. The level of NT pro-brain natriuretic peptide (NT pro-BNP) considered diagnostic of CHF is 1500pg/mL

Treatment

In a patient with pleural effusion secondary to heart failure the preferred treatment is to treat the heart failure with the following drugs:

- digitalis
- diuretics – to reduce preload and
- dilators - to reduce afterload .

The pleural effusion disappears if we manage heart failure successfully. In most patients with heart failure, the pleural effusion is effectively managed only with above management.

Occasionally, the patients tend to be very dyspneic, if large pleural effusion is present. Such persons may get rapid relief from the dyspnea if about 0.5L to 1.0L of pleural fluid is removed. Sometimes therapeutic thoracocentesis is indicated to get symptomatic relief in patients with heart failure and large pleural effusions that are refractory to treatment. So consider interventions to control the pleural effusions in such patients.

2. Hepatic Hydrothorax

One of the complications of hepatic cirrhosis is pleural effusion. But only when ascitic fluid is present, pleural effusion occurs which is called as hepatic hydrothorax.

Pathophysiology

It is evident from the foregoing studies that ascitic fluid is the origin of pleural fluid in these patients.

The fluid in the peritoneal cavity passes directly through the defects in the diaphragm to the pleural space, The diaphragm may be stretched in patients with tense ascites, causing microscopic defects. This is because of the increased intraabdominal pressure, There is always a one-way transfer of fluid from the peritoneal to the pleural cavity in patients with ascites. This is because of increased hydrostatic pressure in the ascitic fluid.

In some patients, the lymphatics play an important role in the production of the pleural effusion. The mechanism behind this is the transfer of ascitic fluid across the diaphragm by the lymphatic vessels.

Therefore, the dominant mechanism of hepatic hydrothorax is the direct movement of fluid across the diaphragm.

Clinical Manifestations

The clinical pictures of cirrhosis and ascites dominate in patients with pleural effusion secondary to cirrhosis. At times, in association with large pleural effusions, these patients develop acute dyspnoea. Although the pleural effusions may be small to moderate in size, they are frequently large and occupy the entire hemithorax. The diaphragmatic defect permits fluid to flow into the pleural cavity from the

peritoneal cavity until the pleural pressure approaches the peritoneal pressure and this results in development of large pleural effusion.

Diagnosis

It is usually easy to diagnose the pleural effusion that is secondary to cirrhosis with ascites. We should perform both a paracentesis and a thoracocentesis. This is to confirm that the ascites and pleural fluid are compatible with the diagnosis. Also to ascertain that they do not have high polymorphonuclear cell counts.

The pleural fluid is occasionally blood tinged or is frankly bloody. But such findings have no significance due to the poor coagulation status of the patient. The differential cell count is dominated by polymorphonuclear leukocytes, small lymphocytes, or other mononuclear cells.

To rule out pancreatic ascites amylase levels should be determined. Also a cytologic examination should be performed to rule out malignant disease. This should be done in both pleural fluid and ascitic fluid.

3. Nephrotic Syndrome

Nephrotic syndrome is common in patients with pleural effusion.

Mechanism

The" combination of increased hydrostatic pressure and decreased plasma oncotic pressure" is the mechanism responsible for the transudative pleural effusion in patients associated with the nephrotic syndrome.

Diagnosis

In the typical clinical situation, it is not difficult to diagnose pleural effusion secondary to nephrotic syndrome. But to confirm that the pleural fluid is indeed a transudate, a diagnostic thoracocentesis should be performed.

In patients with the pleural effusion and nephrotic syndrome, the possibility of pulmonary embolism should always be considered. In all patients with the pleural effusion and nephritic syndrome, one should always obtain a lung scan or a CT angiogram.. It is important that evidence of deep venous thrombosis should be sought with venogram, pulmonary arteriogram or impedance plethysmogram, if the lung scan or spiral CT scan is equivocal.

EXUDATIVE PLEURAL EFFUSION

MOST COMMON CAUSES ARE

1. Parapneumonic pleural effusion
2. Pleural effusion related to metastatic malignancies
3. Tuberculous pleural effusion

1. METASTAIC MALIGNANCIES AND PLEURAL EFFUSION:

The exudative pleural effusion secondary to malignant disease involving the pleura is the second leading cause of exudative pleural effusion. Parapneumonic effusion ranks first in this category.

Common carcinomas associated with malignant pleural effusions are:

1. Lung carcinoma
2. Breast carcinoma
3. Lymphoma
4. Ovarian carcinoma
5. Sarcoma

Rarely carcinoma of uterus, cervix, stomach , colon , pancreas , bladder

MECHANISM

1. Direct mechanism:

a. Increased permeability due to pleural metastasis

b. Obstruction of the pleural lymphatic vessels caused by pleural metastasis

c. Decreased pleural lymphatic drainage and mediastinal node involvement

d. Chylothorax – thoracic duct interruption

e. Decreased pleual pressure – bronchial obstruction

f. Due to involvement of pericardium

2. Indirect mechanism:

a) Pulmonary embolism

b) Postobstructive pneumonitis

c) Hypoproteinemia

d) Postradiation therapy

CLINICAL MANIFESTATIONS

The most common symptom in patients with malignant pleural effusion is dyspnea. Also the symptoms due to the underlying disease will predominate. The symptoms due to underlying malignancy are weight loss, malaise, anorexia. The other manifestations are chest pain, hemoptysis, cough in patients with lung malignancy, breast mass in carcinoma breast, swelling in neck, axilla inguinal regions with mass in the abdomen in case of lymphomas.

Chest radiograph: Besides the pleural effusion, pulmonary abnormalities are demonstrated in patients with pleural effusion secondary to carcinomas. Also there is involvement of mediastinal lymphadenopathy . The pulmonary abnormalities are:

a) pleural nodularity ,

b) pleural rind ,

c) mediastinal pleura involvement ,

d) pleural thickening > 1 cm

Pleural fluid analysis

- Grossly bloody with RBC count > 100,000/mm3.
- WBC count between 1,000 to 10,000 / mm3 with lymphocytes 45 % other mononuclear cells > 40% , polymorphonuclear cells 15 % .
- Reduced pleural fluid glucose level less than 60 mg/ dl.
- Pleural fluid pH below 7.3
- Cytology: It is used to classify the histological subtype like adenocarcinoma but not the primary site of tumour.

- Immunohistochemical tests: Carcinoembryonic antigen is detected in metastatic adenocarcinoma and also stains MOC 3,1,B72.3,Ber – EP4 and BG – 8. Malignant mesothelial cells stain positive for cytokeratin and calretin.
- Tumormarkers: Carcinoembyronic antigen (CEA), carbohydrate antigen (CA) 15 – 3, 19 – 9, 549 and 72.Neuron specific enolase ,SCC antigen , SSEA – sialyl state specific mouse embryonic antigen, cytokeratin 19 fragments .

Non-invasive test

This includes measurement of oncogenes, lectin binding, FISH, flow cytometry, proteomics, chromosomal analysis and hyaluronic acid.

But the only test that is advised is flow cytometry. This is done when a lymphoma is suspected. The diagnosis of lymphoma is done by showing the clonality of lymphocytes in pleural fluid.

Pleural biopsy – CT guided or via thoracoscopy

TREATMENT:

In the management of pleural effusion due to metastatic disease the important thing is to identify the site of primary. This is to decide whether the primary tumor responds to systemic chemotherapy or not. Because some tumours like breast carcinoma, lymphoma, small cell carcinoma respond to systemic chemotherapy very well.

Also intrapleural chemotherapy with cisplatin, staphylococcus aureus super antigen (SSAg), rituximab, interferon – gamma, tumour necrosis factor, interleukin[IL -2] has been tried with varying results.

In patients with malignant pleural effusion and a chylothorax, malignancy usually involves the thoracic duct. So in these patients it is good to administer radiotherapy to the mediastinum.

We have to consider removal of the pleural fluid if the tumor is not responding to chemotherapy or fails to respond to treatment. This is done mainly to relieve the dyspnea.

The procedures available for the chemotherapy resistant pleural effusion are:

1. Indwelling pleural catheter (pleur X)
2. Pleurodesis
3. Intercostal drainage
4. Pleuroperitoneal shunt
5. Repeated thoracentesis
6. Pleurectomy

2. TUBERCULOUS PLEURAL EFFUSION

The development of pleural effusion in a patient with absence of radiologically apparent TB indicates that it would be a sequelae to the primary infection that occurred 6 to 12 weeks before or it may be due to reactivation of TB.

Pathogenesis

In tuberculous patients there are subpleural caseous foci. Tuberculous pleural effusion occurs due to rupture of the subpleural caseous focus in the lung to the pleural space.

In the development of tuberculous pleural effusion the delayed hypersensitivity plays a major role. There is clonal expansion of lymphocytes sensitised to the tuberculous protein. Initially the macrophages predominate in the pleural fluid from day 2 to day 6 and then the lymphocytes predominate in the pleural fluid.

It is clear that the delated hypersensitivity increases the permeability of pleural capillaries to protein. There is higher rate of pleural fluid formation due to the increased levels of pleural fluid protein. Also there is increased level of VEGF, which also increases the permeability. This leads to the accumulation of pleural fluid and development of pleural effusion.

Also there is decrease in the clearance of proteins in the pleural space. This is because of the impedence to the clearance of proteins by the lymphatics as a result of delayed hypersensitivity reactions.

Clinical manifestation:

Patients with pleural TB have symptoms such as fever, dry cough, pleuritic chest pain and dyspnea.

Physical findings are those of pleural effusion such as dullness on percussion and absence of breath sounds.

In HIV individuals there will be longer duration of illness. The incidence of chest pain is low, but night sweats, fatigue, diarrhoea, hepatomegaly, lymphadenopathy , splenomegaly are more common.

They have associated parenchymal lesions, smear for acid fast bacilli positive and also culture positive for AFB.

DIAGNOSIS

Tuberculin skin testing: Tuberculin skin testing is almost always positive if performed after 8 weeks of development of symptoms. So a negative skin testing after 8 weeks of development of symptoms can be used to rule out TB. However in malnourished individuals or HIV patients the test remains negative.

Pleural fluid analysis

1. Pleural fluid protein elevated and usually above 5 g/dL
2. Differential WBC count has more than 50% lymphocytes. If there are eosinophils, it suggests previous thoracentesis or associated pneumothorax.
3. Mesothelial cells not more than 5 %
4. Adenosine deaminase levels more than 70 U/L
5. Interferon gamma levels more than 3.7IU/ml
6. Low pleural fluid pH and CRP levels more than 30 mg/dl

7. Pleual biopsy – demonstration of parietal pleura granuloma, AFB, caseous necrosis.
8. Pleual fluid AFB staining and culture for mycobacteria

3. Parapneumonic effusion:

When any pleural effusion is associated with bacterial pneumonia, lung abscess or bronchiectasis, it is called as parapneumonic effusion.

An empyema is defined as pus in the pleural space. Many complicated parapneumonic effusions are usually in the form of empyema.

According to Weese et al. empyema is charecterised by specific gravity greater than 1.018 , protein more than 2.5 g/dL , WBC count more than 500 cells/ mm3 But according to Vianna empyema is defined as pleural fluid protein more than 3.0 g/dL , WBC greater than 15000 / mm3 or positive bacterial cultures.

Pathogenesis

1. Exudative stage

This stage is characterised by rapid accumulation of sterile pleural effusion. Due to increased capillary permeability, the fluid originates from the interstitial spaces of lung and also from the visceral pleural capillaries. There is low WBC count, low LDH level and a normal glucose level in the pleural fluid at this stage. This stage resolves if appropriate antibiotics are instituted.

2. Fibropurulent stage

The pleural space is invaded by the bacteria if antibiotics are not intiated. In this stage there is accumulation of large amounts of pleural fluid which is rich in bacteria, polymorphonuclear leucocytes and cellular debris. A continuous sheet of fibrin covers the visceral and parietal pleura. This leads to the loculation and prevents the spread of pus. But this makes the insertion of chest tube difficult. In this stage there is higher pleural fluid LDH and lower pleural fluid glucose and pH

3. Organisation stage

This stage is characterised by pleural peel. The fibroblasts grow in to the exudates and an inelastic membrane is produced. The lung is encased by this inelastic pleural peel and makes it functionless. The exudate is thick at this stage and it may spontaneously drain through the chest wall called as empyema necessitans or into the lung producing a broncho-pleural fistula.

The most common organisms are Staphylococcal aureus, Escherichia coli and anaerobic Bacterioids.

Clinical features

Fever, cough with expectoration, chest pain are the major symptoms. Fever may be absent in immune-compromised patients. If the fever is present for more than 48 hours after the institution of antibiotics it is called as parapneumonic effusion. It is important to elicit history of alcoholism, seizures or an episode of unconsciousness as it leads to aspiration.

Light's classification for parapneumonic effusions and empyema:

1. Non-significant pleural effusion
2. Typical parapneumonic pleural effusion
3. Borderline complicated pleural effusion
4. Simple complicated pleural effusion
5. Complex complicated pleural effusion
6. Simple empyema
7. Complex empyema

Diagnosis

1. During thoracocentesis, there is frank pus.
2. The pleural fluid will be positive for Gram stain & culture.
3. Pleural fluid glucose less than 40 mg / dL , pH < 7.0 , LDH > 3 times the upper limit.

The above findings along with loculations constitute bad prognostic factors for both empyema and parapneumonic effusions.

Management

Antibiotics

Community acquired pneumonia:

- Fluroquinolones such as levofloxacin, moxifloxacin, gatifloxacin or a macrolide such as azithromycin, clarithromycin plus beta lactams such as cefotaxime, ceftriaxone, ampicillin – sulfbactam .

- If pseudomonas is suspected anti pseudomonas antibiotics like meropenem, imipenem, piperacillin-tazobactam or cefepime is used.

Anaerobes – metronidazole or clindamycin.

MRSA – vancomycin

Management for pleural effusions

1. Therapeutic thoracocentesis
2. Tube thoracostomy
3. Intrapleural fibrinolytics like streptokinase, streptodornase, tissue plasminogen activator
4. Video assisted thoracoscopy with lysis of adhesions and / or decortication
5. Decortication
6. Open drainage

MATERIALS AND METHODS

MATERIALS AND METHODS

STUDY POPULATION

This study is to be conducted among 60 patients with pleural Effusion, attending the Department of Medicine & Department of Thoracic Medicine in Govt. Rajaji Hospital, Madurai.

Inclusion Criteria

- In Patients with clinical and radiological evidence of pleural effusion irrespective of etiology, both sex
- Age > 12 years

Exclusion criteria

- Age less than 12 years
- Pregnancy
- GOUT
- HEMOTHORAX

ANTICIPATED OUTCOME:

Pleural fluid Uric acid and ratio to serum levels is superior or supportive to Light's criteria in differentiating transudates and exudates.

DATA COLLECTION

- "A Brief history with clinical examination will be done.
- Detailed Clinical Examination,

- Pleural fluid Uric acid, Serum Uric acid , Pleural fluid total protein, Serum total protein , Pleural & Serum LDH are estimated."

LABORATORY INVESTIGATIONS

1. Pleural fluid Uric acid & Serum Uric acid
2. Pleural fluid total protein & Serum Protein
3. Pleural fluid LDH & Serum LDH

DESIGN OF STUDY

Prospective analytical study

PERIOD OF STUDY

March 2017 to September 2017

COLLABORATING DEPARTMENTS:

Department of Medicine, Department of Thoracic medicine , Department of Biohemistry

CONSENT: Individual written and informed consent.

ANALYSIS: Statistical analysis

CONFLICT OF INTEREST: Nil

METHOD OF STUDY

This study was conducted in Govt. Rajaji Hospital, Madurai. This study subjects were chosen from the patients admitted in Department of Medicine and Department of Thoracic Medicine, Govt. Rajaji Hospital Madurai.

The study was conducted in 60 patients; the patients had pleural effusion with clinical background of congestive cardiac failure, chronic hepatic disease, chronic kidney disease, tuberculosis, parapneumonic effusions, malignancy.

The patients are examined clinically with the following parameters and 60 cases are taken for study.

Clinical criteria to classify patients as exudates and transudative pleural effusion

If the patient had oedema legs, ascites, cardiac enlargement, radiological evidence of congested lungs and responded to treatment for congestive cardiac failure, then the diagnosis of congestive cardiac failure was made.

When there were raised serum urea and creatinine levels along with facial puffiness, pallor, USG evidence of contacted kidney, chronic kidney disease was diagnosed.

If the patient had features of liver cell failure, ascites, spleenomegaly and evidence of volume overload status, chronic liver disease was diagnosed.

The diagnosis of tuberculosis was made if there is cough , fever with evening rise of temperature, loss of weight and appetite ,sputum showing AFB, ADA in pleural fluid ,chest x ray showing pleural effusion ,response to ATT.

The diagnosis of parapneumonic effusion was made if there is cough with expectoration, fever with chills & rigors, chest x-ray showing pleural effusion, bacteria in pleural fluid/sputum.

The diagnosis of malignant pleural effusion was made if there is positive pleural fluid cytology, Pleural biopsy, demonstration of primary sites.

Study protocol

- Patients with clinical and radiologicaly diagnosed cases of pleural effusion are included in this study
- Then they are classified in to exudates and transudates on the basis of the clinical , radiological and biochemical evaluation .
- In all the patients following investigation are done to classify them as exudates and transudates
- Pleural fluid uricacid & Serum uric acid , Pleural fluid total protein ,LDH and serum protein,LDH are estimated and the patients are classified in to exudates and transudates.
- Then the patients are classified in to exudates and transudates on the basis of Light's criteria.
- Now the classification of exudates and transudates done on the basis of Total Pleural fluid uric acid and its ratio to serum , Pleural fluid Total protein are compared with results of the classification of exudates and transudates done on the basis of Light's criteria.
- For each testSensitivity , specificity , Positive predictive value , negative predictive value , diagnostic accuracy are calculated .

RESULTS AND INTERPRETATION

RESULTS AND INTERPRETATION

Age and sex distribution of the population in our study is as follows

41.67% of the study subjects were in the age group of 56-70yrs, 35% were in the age group of 41-55yrs, 18.2% were less than 40 years and 5.07% above 70 years.

Majority of the study subjects were males 60% while remaining 40% were females.

Exudates and transudates distribution in our study is as follows:

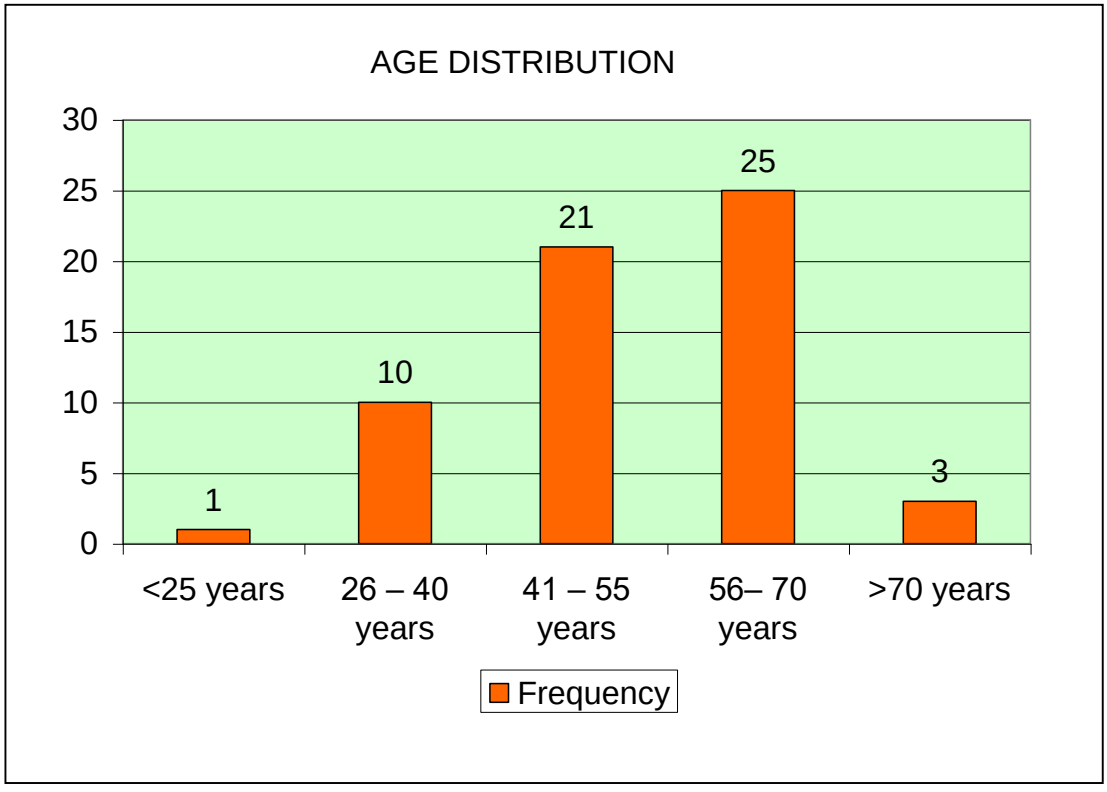
In our study about 55% of the study subjects were exudates while 45% were transudates.

Among the study group, about 33.3 % of study groups have tuberculosis , 15 % have malignancy and6.7 % have parapneumonic effusions.

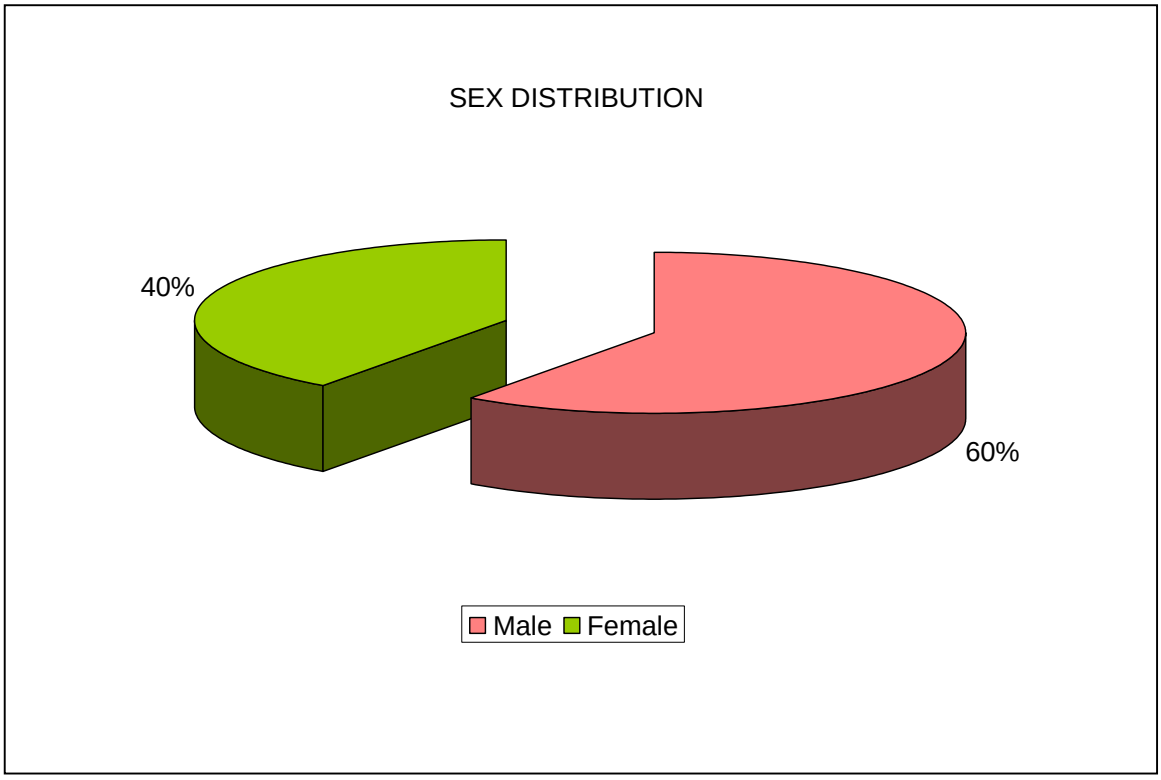
15% were CCF,15% were CKD and the remaining 15% were Hepatic hydrothorax.

Pleural fluid Uric acid, Serum Uric acid, Pleural fluid total protein , Serum total protein , Pleural fluid LDH , Serum LDH are estimated..

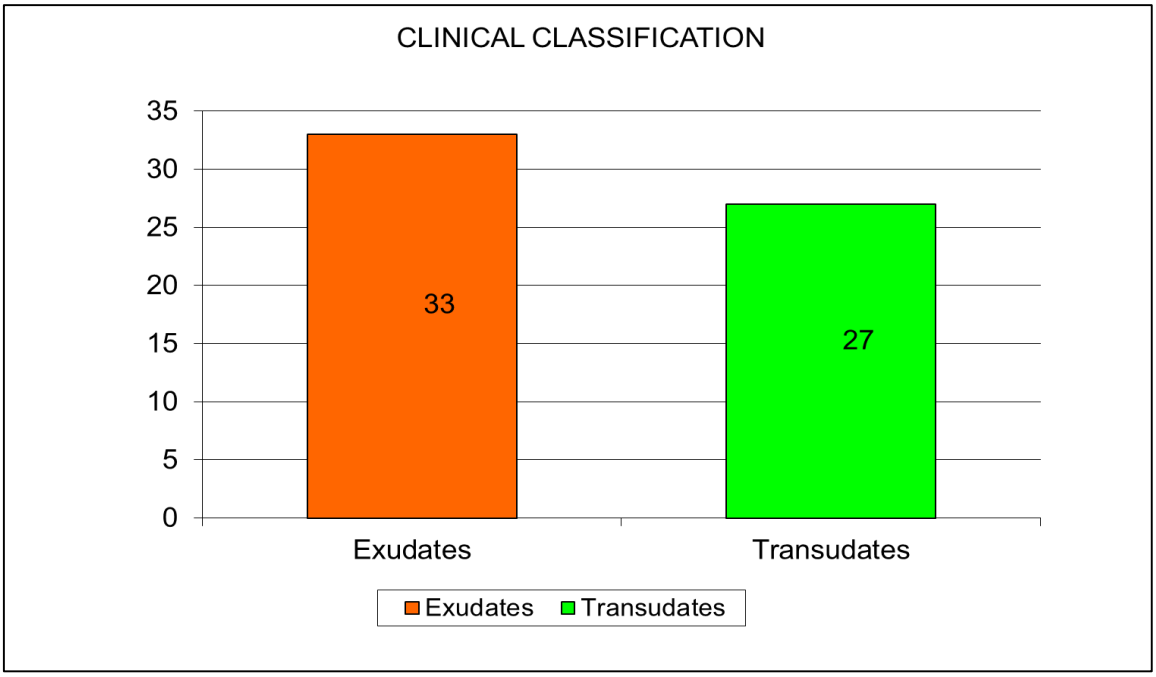
Age group	Frequency	Percent
<25 years	1	1.66
26 – 40 years	10	16.66
41 – 55 years	21	35.00
56– 70 years	25	41.67
>70 years	3	5.01
Total	**60**	**100.00**



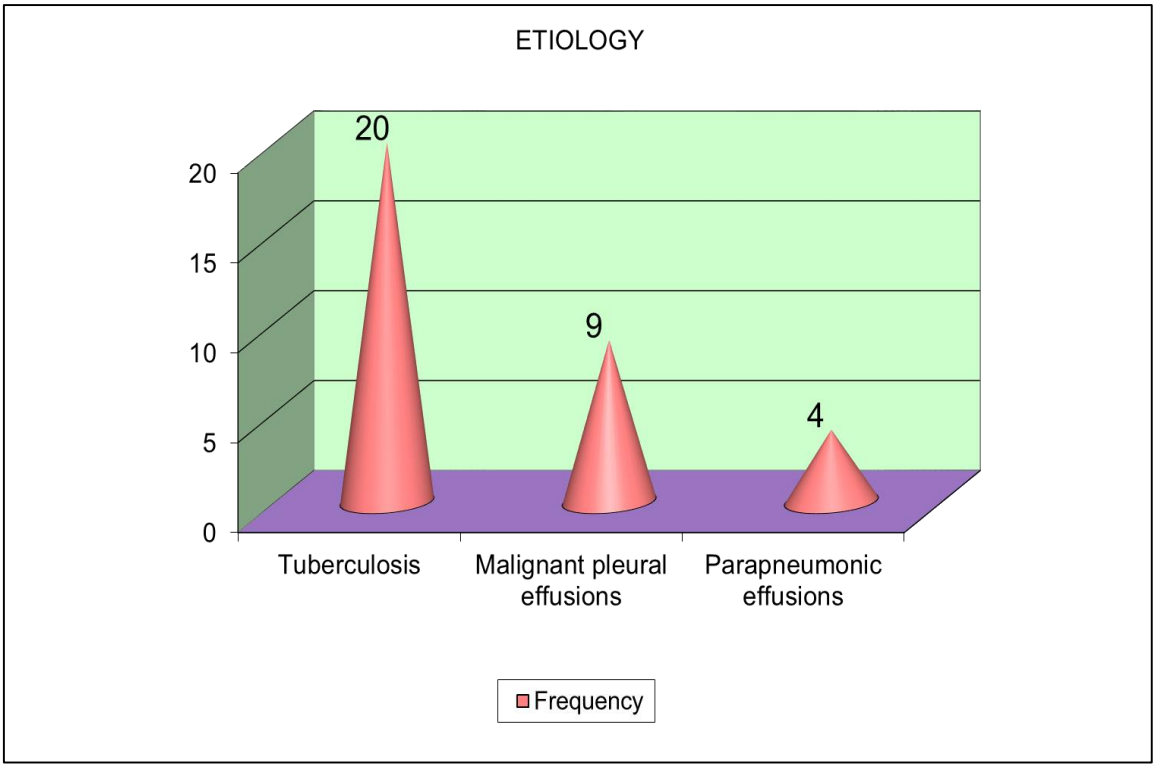
Gender	Frequency	Percent
Female	24	40.0
Male	36	60.0
Total	60	100.0



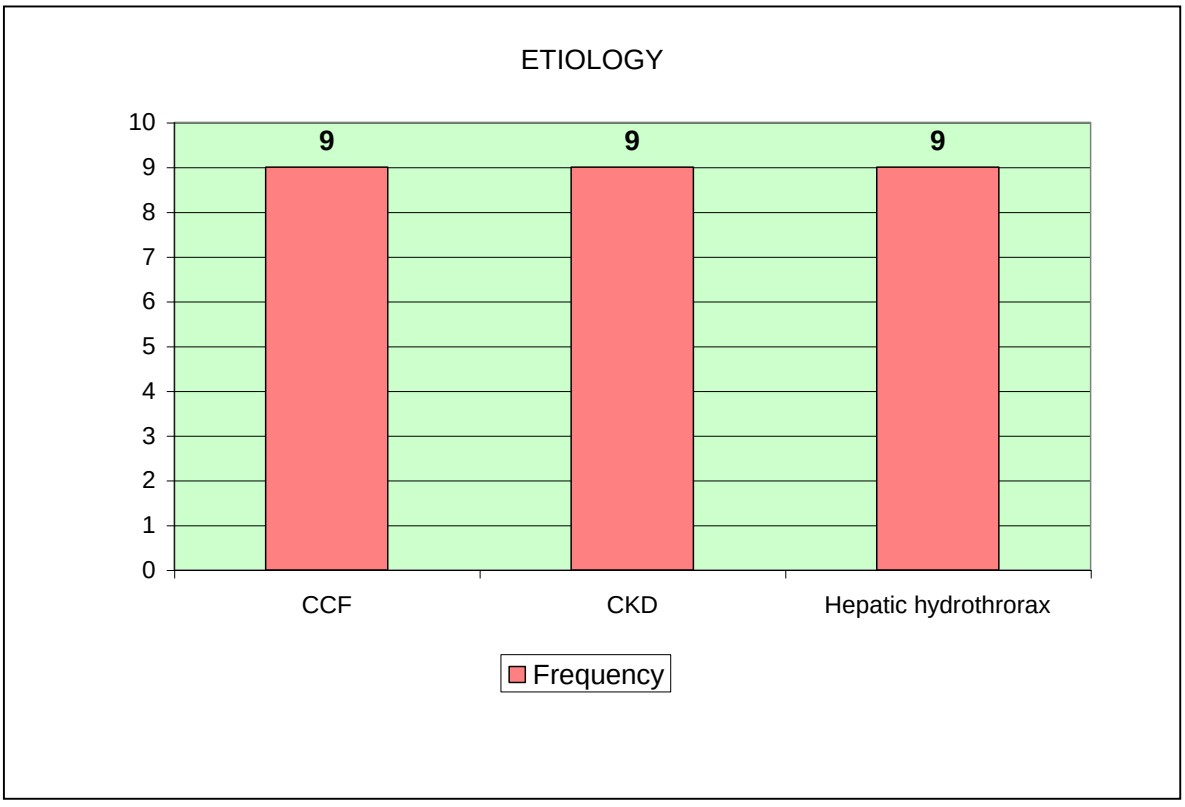
Clinical classification	Frequency	Percent
Exudates	33	55.00
Transudates	27	45.00
Total	60	100.00



Etiology	Frequency	Percent
Tuberculosis	20	33.3
Malignant pleural effusions	9	15.0
Parapneumonic effusions	4	6.7



Etiology	Frequency	Percent
CCF	9	15.0
CKD	9	15.0
Hepatic hydrothrorax	9	15.0
Total	27	45.0

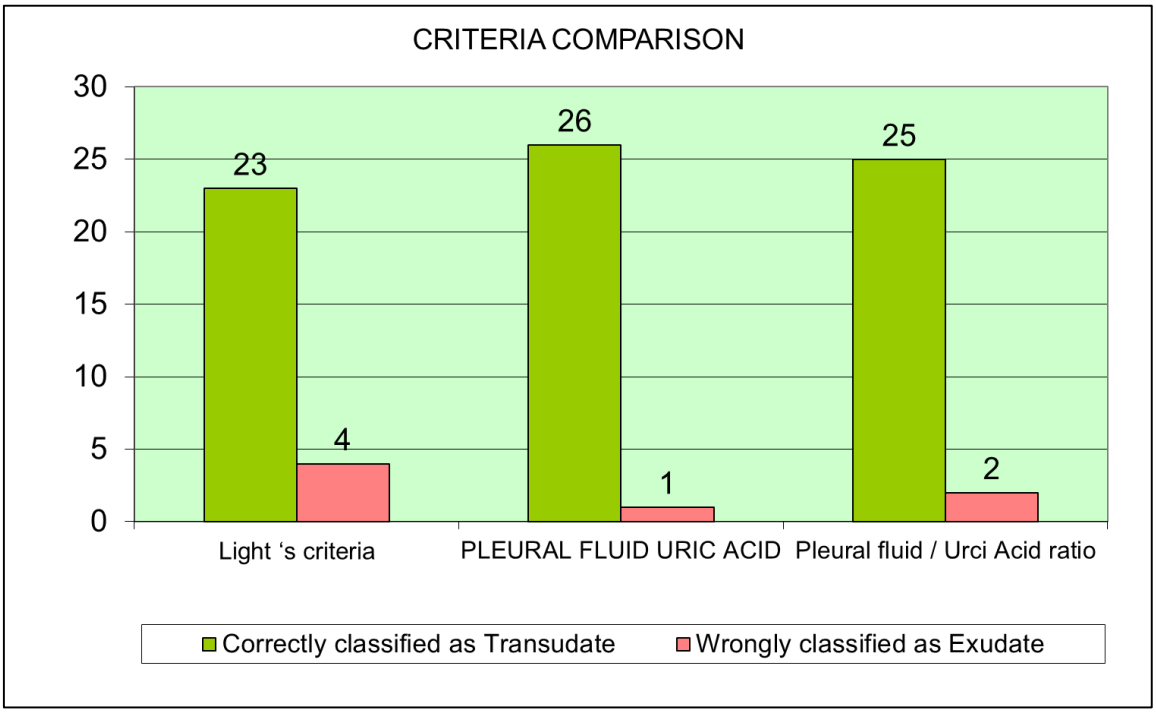


ETIOLOGY DISTRIBUTION

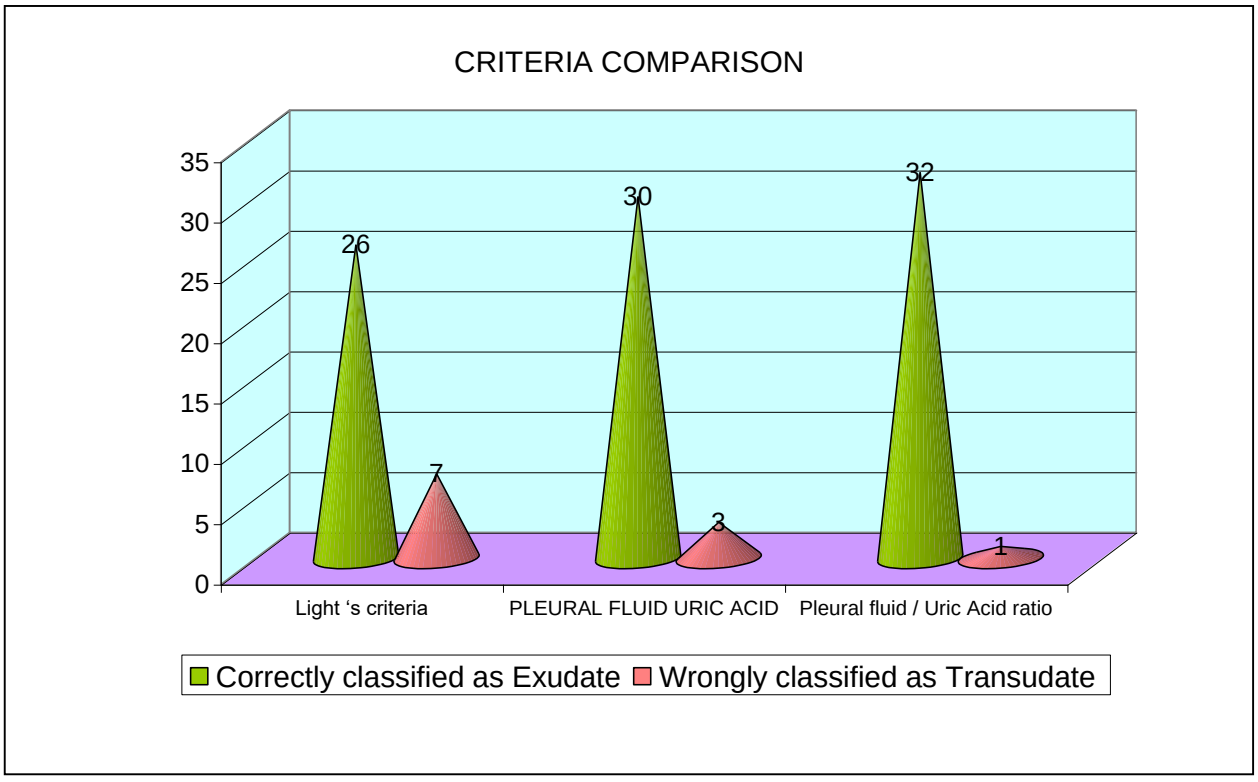
Etiology	Frequency
Tuberculosis	20
Malignant pleural effusions	9
Parapneumonic effusions	4
CCF	9
CKD	9
Hepatic hydrothrorax	9
Total	60

Descriptive Statistics	Min	Max	Mean	SD
Pleural fluid protein	2.11	4.45	3.04	0.56
Serum protein	5.22	6.81	6.12	0.41
Pleural fluid / Serum protein ratio	0.32	0.71	0.49	0.12
Pleural fluid LDH	19.1	342	105.3	78.84
Serum LDH	79.1	486	191.58	100.12
Pleural / Serum LDH Ratio	0.22	0.79	0.49	0.16
Pleural fluid Uric acid	3.69	10.57	6.06	1.99
Serum Uric acid	11.06	16.78	14.10	1.12
Plerual fluid / serum Uric acid ratio	0.23	0.63	0.43	0.12

Criteria	Correctly classified as transudate N (%)	Wrongly classified as exudate N (%)
Light 's criteria	23 (85.2%)	4 (14.8%)
PLEURAL Fluid Uric Acid	26 (96.3%)	1 (3.7%)
Pleural fluid / Serum Uric acid Ratio	25 (92.6%)	2 (7.4%)



Criteria	Correctly classified as Exudate N (%)	Wrongly classified as Transudate N (%)
Light ‘s criteria	26	7
Pleural Fluid Uric Acid	30	3
Pleural fluid / Serum Uric Acid Ratio	32	1



Pleural fluid Uric acid	Mean	SD	p value
Exudate	4.43	0.49	<0.001 Significant
Transudate	8.05	1.1	

Serum Uric acid	Mean	SD	p value
Exudate	13.8	1.13	0.019 Significant
Transudate	14.47	0.99	

Pleural fluid /Serum Uric acid Ratio	Mean	SD	p value
Exudate	0.33	0.06	< 0.001 Significant
Transudate	0.55	0.04	

RESULTS

By applying Light's criteria in patients with exudative pleural effusion classified clinically, 78.8% % of the cases were correctly diagnosed as exudative pleural effusion.

By applying Pleural fluid Uric acid in patients with exudative pleural effusion classified clinically, 90.9% of the cases were correctly diagnosed as exudative pleural effusion.

According to Pleural fluid/Serum Uric acid ratio, patients with exudative pleural effusion classified clinically, 96.9% of the cases were correctly diagnosed as exudative pleural effusion.

In our study by applying the Lights criteria, about 21.2 % of exudative pleural effusion was misclassified as transudative, and by applying Pleural fluid Uric acid, the misclassification was 9.1% .Whereas by Pleural fluid / Serum Uric acid ratio, the misclassification was only 3.10 %.

By applying Light's criteria in patients with transudative pleural effusion classified clinically, 85.2 % of the cases were correctly diagnosed as transudative pleural effusion.

By applying Pleural fluid Uric acid in patients with transudative pleural effusion classified clinically, 96.3 % of the cases were correctly diagnosed as transudative pleural effusion.

According to Pleural fluid / Serum Uric acid ratio , in patients with transudative pleural effusion classified clinically, 92.6 % of the cases were correctly diagnosed as transudative pleural effusion.

Among the parameters used most specific test to classify an transudative pleural effusion from a exudativee pleural effusion is pleural fluid uric acid which is 96.3 % and most sensitive test is pleural fluid / serum uric acid ratio which is 96.96 %. The positive predictive value, negative predictive value and diagnostic accuracy to classify an exudative pleural effusion from a transudative pleural effusion is higher for pleural fluid uric acid which is 96.29 % , 95.23 % , 94 % respectively.

The sensitivity, specificity, positive predictive value, negative predictive value and diagnostic accuracy of Light's criteria are 86.71 %, 91.90 %, 92.30 %, 84.33 %, 88.1% respectively.

DEFINITIONS

Diagnostic accuracy: This is the probability that a randomly selected subject is correctly diagnosed by the test.

Negative Predictive Value: The probability that a person who has tested negative on a diagnostic test (T−) actually does not have the disease (D−)

Positive Predictive Value : This is the probability that a person who has tested positive on a diagnostic test (T+) actually has the disease(D+).

Sensitivity : This is the probability that a person with disease (D+) will correctly test positive based on the diagnostic test (T+)

Specificity: This is the probability that a person without disease (D−) will correctly test negative based on the diagnostic test (T−)

D – Disease ., T – Test

DISCUSSION

DISCUSSION

One of the most common disease entity encountered by physicians worldwide is pleural effusion. In a situation where undiagnosed pleural effusion has come across, the first and foremost thing to be determined is whether the fluid is a transudate or exudate. The most commonly used Light's criteria, though still considered as a gold standard, often misclassify a 25% of transudate as an exudates in certain situation like congestive cardiac failure following diuretic therapy and in patient with pulmonary TB with hypoproteinemia. The present study was undertaken to evaluate the efficacy of pleural fluid Uric acid and its ratio to serum levels, in distinguishing pleural fluid transudates and exudates and its correlation with Light's criteria and was found to be more useful in these situations..

Metintas et al[15] reported that levels of uricacid is increase more in transudative pleural fluid (CCF, peritoneal dialysis, cirrhosis and nephrotic syndrome) than as comparatively to exudative condition. , In exudative condition the local factors influencing the accumulation of pleural fluid are altered. Exudates involve increased capillary permeability and lymphatic obstruction.

Whereas transudates are the result of changes in hydrostatic forces [imbalances in hydrostatic and oncotic forces], with capillary permeability remaining normal".

The condition which produces transudative pleural effusion exerts much oxidative stress and hypoxia in the tissue .It is stated that increases in uric acid may be found in clinical conditions associated with tissue hypoxia.

Uzen et al[9] had shown that the mean pleural fluid uric acid levels vary significantly between exudates and transudates with the specificity and sensitivity of pleural fliud uric acid for diagnosis of transudative effusion being73% and 80.6% respectively,

BasanthaHazarika et al[15] reported that the increase uric acid level was observed in pleural fluid of transudative pleural effusion than exudative pleural efussion and the optimum cut off level for pleural fluid uricacid was 5.35mg/dl with sensitivity of 89.32% and specificity of 92.60%.

Ashish Jain1, Raina Jain et al reported that".increase Uric acid level was observed in pleural fluid of transudative pleural effusion than exudative pleural effusion". It was also observed that the" level of uric acid was more in pleural fluid than serum and ratio (pleural fluid / serum) of uric acid was ≥1 in transudative conditions but in case of exudative condition the this ratio was < 1". The optimum cut-off level for P uric acid was 5.5 mg/dl with sensitivity of 94.00% and specificity of 83.00%. The optimum cut-off levels for P/S uric acid ratio was 1.0 with sensitivity of 96.00% and specificity of 92.16%.

In our study to diagnose transudate the following parameters are used

- A pleural fluid Uric acid of more than 5.45 IU
- A pleural fluid Uric acid to serum Uric acid ratio of more than 0.45,
- A pleural fluid total protein less than 3.03mg
- A pleural fluid pritein to serum protein ratio less than 0.49

According to Pleural fluid/Serum Uric acid ratio, patients with exudative pleural effusion 96.9% of the cases were correctly diagnosed as exudative pleural effusion.

CONCLUSION

CONCLUSION

For many decades Light's criteria had been used widely to differentiate exudative from transudative pleural effusion. But it also misclassified 25 % of transudates as exudates, so there was a need to identify new parameters which would prove to be superior or supportive to the array of tests at present.

From our study we came to known that there was statistically significantcriteria in classifying pleural effusion as exudates and transudates.

The misclassification of exudates and transudates by various criteria when compared to Light's criteria is statistically significant as p value is <0.001.

From our study we came to a conclusion that to classify transudative pleural effusion from a exudative pleural effusion

- most specific test is pleural fluid uric acid and
- most sensitive test is pleural fluid / serum uric acid ratio .

The positive predictive value, negative predictive value and diagnostic accuracy is higher for pleural fluid uric acid.

To conclude, though Light's criteria remains as gold standard to differentiate transudates and exudates, in cases where there is a mismatch between clinical diagnosis and the outcome from Light's criteria, pleural fluid Uric acid / serum Uric acid ratio and pleural fluid uric acid evaluation may add to the diagnostic accuracy.

SUMMARY

The classic criteria of differentiating an exudate from a transudate is Light's criteria. Over the last few years, it has been noted that even Light's criteria may misclassify a significant percentage of pleural effusions.

The objective of the present study was to evaluate the usefulness of Total Pleural fluid Uric acid and its ratio to serum levels and Pleural fluid Total Protein level in classifying pleural effusions as exudates and transudates with Light's criteria as the gold standard

From our study it is evident that most specific test to classify a transudative pleural effusion from an exudative pleural effusion is pleural fluid uric acid which is 96.3 % and most sensitive test is pleural fluid / serum Uric acid ratio which is 96.9 %. The positive predictive value, negative predictive value and diagnostic accuracy is higher for pleural fluid uric acid which are 96.29%, 95.23 %, 94 % respectively.

The sensitivity, specificity, positive predictive value, negative predictive value and diagnostic accuracy of pleural fluid Uric acid was superior to Light 's criteria.

The pleural fluid/serum uric acid ratio, pleural fluid total protein are very effective in differentiating exudative and transudative pleural effusion.

LIMITATIONS OF THE STUDY

Limitations of the Study

1. Shorter study period and smaller study sample
2. The various parameters studied are neither combined with others nor with the Light's criteria.

Further Recommendations

1. A longer study period and a larger study sample should be considered in the future.
2. Combination of Pleural fluid uric acid, Pleural fluid / Serum uric acid ratio, Pleural fluid total protein with other parameters of the Light's criteria.

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BIBLIOGRAPHY

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PROFORMA

PROFORMA

Name : **Age/Sex/Occupation:**

Presenting complaints:

H/o Fever, chest pain, cough & expectoration, hemoptysis ,dyspnea, Loss of weight, Loss of Appetite. Etc.

Past history:

H/o Tuberculosis, Chronic liver disease, coronary artery disease, chronic kidney disease

Clinical examination:

General examination:

Consciousness, Pallor, jaundice, Clubbing, Lymphadenopathy, Vitals: PR, BP, RR, SpO2, Temperature

Systemic examination:

CVS:

RS:

Abdomen:

CNS:

LABORATORY INVESTIGATIONS:

1. Pleural fluid Uric acid & serum Uric acid
2. Pleural fluid total protein & Serum Protein
3. Pleural fluid LDH & Serum LDH

MASTER CHART

MASTER CHART

S. No	Name	Age	Sex	Diagnosis	Pleural Fluid Protein g/ dl	Serum Protein g/dl	Pleural Fluid Protein / Serum Protein Ratio	Pleural Fluid LDH	Serum LDH	Pleura L Fluid / Serum LDH Ratio	Pleura L Fluid Uric Acid	Pleural Fluid: Serum Uric Acid Ratio
1	ESWARI	40	F	CCF	2.7	6.1	0.44	156	306	0.51	10.57	0.63
2	NARAYANAN	59	M	CCF	2.9	5.6	0.51	132	288	0.45	9.07	0..59
3	LAKSHMI	43	F	CCF	2.9	6.4	0.45	45	159	0.28	8.81	0..58
4	PERUMAL	52	M	CCF	2.5	6.2	0.4	116	250	0.46	8.35	0..57
5	VIJAYAKUMAR	62	M	CCF	2.3	6.4	0.35	129	296	0.43	7.93	0..55
6	KASI	55	M	CCF	2.9	6.5	0.44	112	220	0.51	7.55	0..54
7	RAJAMANI	55	F	CCF	2.2	6.5	0.34	28	91	0.31	7.55	0..54
8	INDIRA	37	F	CCF	2.6	6.2	0.42	59	146	0.4	6.90	0..51
9	ARJUNAN	55	M	CKD	2.8	5.2	0.53	98	189	0.51	8.35	0..57
10	KUPPUSAMY	65	M	CCF	2.6	6.1	0.42	57	110	0.51	7.93	0.55
11	RAMJAN	40	M	Hepatic hydrothorax	2.9	6.4	0.45	69	156	0.44	10.57	0.63
12	SUMATHIRA	48	M	Hepatic hydrothorax	2.8	6.5	0.43	116	216	0.53	8.35	0.57
13	RAJARAM	44	M	Hepatic hydrothorax	3.2	6.5	0.49	97	193	0.5	8.81	0.58
14	PANJAVARNAM	45	F	Hepatic hydrothorax	2.6	6.7	0.38	149	320	0.46	9.33	0.60
15	PAKIYAM	46	F	Hepatic hydrothorax	2.3	6.4	0.35	133	287	0.46	9.07	0.59
16	RAJENDRAN	62	M	Hepatic hydrothorax	2.6	5.9	0.44	41	142	0.28	8.81	0.58
17	CHANDRAN	48	F	Hepatic hydrothorax	2.6	5.8	0.43	26	98	0.26	7.93	0.55
18	ARUMUGAM	44	M	Hepatic hydrothorax	2.5	5.7	0.44	35	116	0.31	6.90	0.51
19	MURUGAPPAN	64	M	CKD	2.5	5.9	0.45	19	85	0.22	7.74	0.55

20	MURUGAN	40	M	CKD	2.1	6.5	0.31	56	132	0.42	7.93	0.55
21	SARASU	57	F	CKD	2.1	6.6	0.32	48	124	0.38	6.90	0.51
22	ALAGAMMAL	65	M	CKD	2.3	6.7	0.34	38	106	0.35	8.35	0.57
23	VALLI	63	F	Tuberculosis	3.8	6.1	0.62	79	165	0.47	5.29	0.41
24	GANESAN	41	M	Tuberculosis	3.5	6.1	0.39	100	133	0.38	4.88	0.38
25	MARIMUTHU	58	M	Tuberculosis	4.4	6.1	0.72	45	95	0.47	5.12	0.40
26	RAMASAMY	46	M	Tuberculosis	3.2	5.9	0.54	106	190	0.55	5.01	0.39
27	SELVAM	50	M	Tuberculosis	3.6	6.1	0.59	98	172	0.56	4.07	0.28
28	KALEESHWARI	34	F	Tuberculosis	3.2	5.6	0.57	94	166	0.56	4.53	0.34
29	VEERAYEE	65	F	Tuberculosis	3.3	5.5	0.6	69	124	0.55	4.17	0.30
30	SIGAPPI	69	F	Tuberculosis	4.1	5.9	0.69	71	137	0.51	4.23	0.30
31	JOTHI	42	F	Tuberculosis	3.2	6.8	0.43	58	101	0.42	4.29	0.31
32	MEENATCHI	71	F	Tuberculosis	3.1	5.2	0.59	66	86	0.76	4.67	0.35
33	ALAGARSAMY	38	M	Tuberculosis	3.9	5.9	0.66	298	387	0.77	4.96	0.38
34	KANDAN	59	M	Tuberculosis	3.6	5.3	0.67	250	320	0.78	3.87	0.35
35	SANJAY	24	M	Tuberculosis	4.1	6.1	0.65	114	235	0.48	3.96	0.27
36	PANDIAMMAL	48	F	Tuberculosis	3.1	6.4	0.43	99	219	0.45	3.82	0.25
37	SANTHI	32	F	Pneumonia	3.5	6.5	0.53	306	421	0.72	3.77	0.24
38	SARAVANAN	43	M	Pneumonia	3.2	6.6	0.42	112	216	0.4	3.69	0.23
39	PALANIVEL	40	M	Pneumonia	3.4	6.1	0.56	341	487	0.71	3.77	0.24
40	PIRAMMAN	62	F	Pneumonia	2.9	6.5	0.58	221	362	0.61	4.07	0.28
41	SUBBIAH	65	M	Malignancy	3.2	5.9	0.54	74	116	0.63	4.67	0.35
42	KARUPPIAH	70	M	Malignancy	3.1	5.8	0.53	102	154	0.66	4.96	0.38
43	PARVATHI	62	F	Malignancy	2.7	5.9	0.42	82	198	0.41	3.73	0.23
44	SEENI	72	M	Malignancy	3.4	6.3	0.53	68	85	0.79	4.90	0.38

45	BALU	75	M	Malignancy	3.3	6.1	0.54	41	79	0.51	4.96	0.38
46	PERIYASAMY	64	M	Malignancy	3.1	5.9	0.52	95	166	0.57	5.03	0.39
47	MARIAMMAL	68	F	Malignancy	3.2	5.8	0.54	86	109	0.78	4.96	0.38
48	KOODALINGAM	66	M	Malignancy	3.5	5.6	0.62	56	141	0.39	4.09	0.28
49	KALIMUTHU	68	M	TUBERCULOSIS	3.2	5.8	0.43	112	163	0.42	4.09	0.28
50	RATHINAM	67	F	Malignancy	3.4	6.2	0.54	59	92	0.64	4.96	0.38
51	SEIKDAVOOD	39	M	Hepatic hydrothorax	2.5	5.7	0.44	35	116	0.31	6.86	0.51
52	NAGARAJ	46	M	CKD	2.5	5.9	0.45	19	85	0.22	6.58	0.50
53	PONNUCHAMY	65	M	CKD	2.1	6.5	0.31	56	132	0.42	7.03	0.52
54	SEVAGAN	69	M	CKD	2.1	6.6	0.32	48	124	0.38	6.70	0.51
55	PONNAMMAL	65	F	CKD	2.3	6.7	0.34	38	106	0.35	6.59	0.50
56	VIJAYA	39	F	Tuberculosis	3.9	5.9	0.66	298	387	0.77	4.67	0.35
57	DEIYVANAI	54	F	Tuberculosis	3.6	5.3	0.67	250	320	0.78	4.53	0.34
58	KAILASAM	43	M	Tuberculosis	4.1	6.1	0.65	114	235	0.48	4.40	0.33
59	SOMAN	58	M	Tuberculosis	3.1	6.4	0.41	99	219	0.44	4.07	0.30
60	RAMAYEE	47	F	TUBERCULOSIS	3.5	6.5	0.53	306	421	0.72	4.09	0.28
					3.03	6.11	0.49	105.40	191.57	0.50	5.45	0.42

ETHICAL COMMITTEE APPROVAL LETTER

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MADURAI MEDICAL COLLEGE
MADURAI, TAMILNADU, INDIA -625 020
(Affiliated to The Tamilnadu Dr.MGR Medical University, Chennai, Tamil Nadu)

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Businessman,21, Jawahar Street, Gandhi Nagar, Madurai.

ETHICS COMMITTEE CERTIFICATE

Name of the Candidate : Dr.P.Karuppasamy

Course : PG in MD., General Medicine

Period of Study : 2015-2018

College : MADURAI MEDICAL COLLEGE

Research Topic :

Usefulness of pleural fluid uric acid and its ratio to serum uric acid levels in classifying pleural effusions as exudates and transudates and its correlation with Light's criteria.

Ethical Committee as on : 02.06.2017

The Ethics Committee, Madurai Medical College has decided to inform that your Research proposal is accepted.

Member Secretary

Chairman
Prof Dr V Nagaraajan
M.D., MNAMS, D.M., Dsc.,(Neuro), Dsc (Hon)
CHAIRMAN
IEC - Madurai Medical College
Madurai

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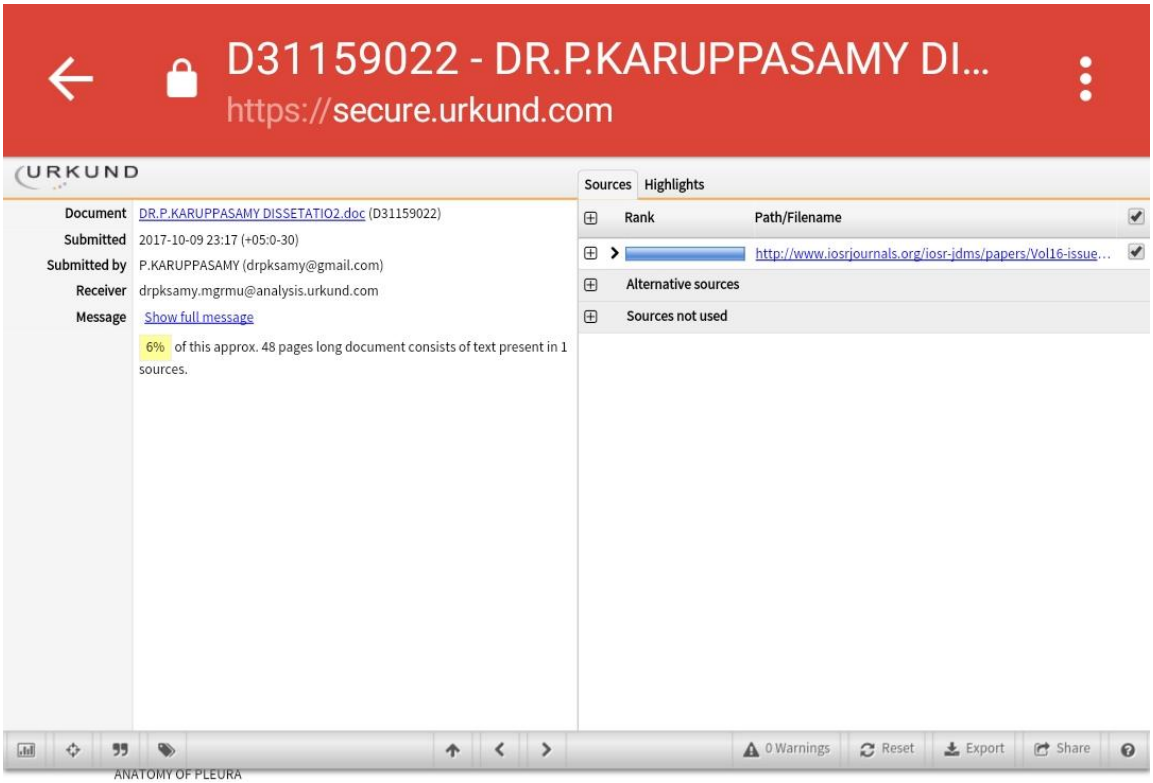

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